PRO-KIIDS "Pediatric Network"

Crohn's and Colitis Foundation of America

Risk Stratification and Identification of Immunogenetic and Microbial Markers of Rapid Disease Progression in Children with Crohn's Disease

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Manual of Study Operations
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Manual of Study Operations

TABLE OF CONTENTS

MANUAL OF OPERATIONS

This Manual of Operations has been created to provide details concerning the design, conduct, performance, monitoring, recording, analysis, and reporting of the study to assure that the data and reporting results are accurate and that the rights, integrity, and confidentiality of the participants are protected.

GENERAL INFORMATION

Background

Children with Crohn's disease show a wide variation in disease activity; some may have mild activity while others have severe disease activity which can lead to poor quality of life, complications and surgery. At this time there are no reliable indicators to predict a more complicated disease course in children first diagnosed with Crohn's disease. This information would be extremely valuable to appropriately tailor more aggressive therapy to children who have a high likelihood of a severe disease course. Currently available therapies alleviate symptoms from the disease, but it is not clear whether any of these treatments modify the natural history of Crohn's disease, and at what time in the progression of disease their introduction would be optimal. The overall goal of this project is to determine clinical parameters and biomarkers that predict progression of disease to the need for surgery as a first step in elucidating these important questions. We will identify factors that mitigate or accelerate disease progression and develop and validate a risk model for predicting severe disease course using state of the art clinical, immune, genetic and bacteriological risk markers in children with newly diagnosed Crohn's disease.

This project will use uniform disease phenotype definitions and an integrated approach for the collection of clinical information, specimen gathering and banking, and storage of data. It is our hope that the analysis of this information will allow us to develop effective tools for disease prognostication, improved therapeutic intervention strategies, and to develop new classes of therapeutics and preventatives.

Data to build a clinical prediction tool to the development of structuring/penetrating Crohn's disease will be obtained in a prospective fashion by a large-scale multi-center collaborative effort. To this end, a Pediatric IBD Research Network has been developed under the auspices of the Crohn's & Colitis Foundation of America which involves a structure under which various institutions will work together on mutually agreed upon multiple projects. This new structure will include CCFA representatives, Network investigators, and an external advisory board that will help steer the initial steps of the network's formation and monitor network activities moving forward.

Crohn's disease - Crohn's disease is a chronic (ongoing) disorder that causes inflammation of the digestive or gastrointestinal (GI) tract. Although it can involve any area of the GI tract from the mouth to the anus, it most commonly affects the small intestine and/or colon.

The disease is named after Dr. Burrill B. Crohn. In 1932, Dr. Crohn and two colleagues, Dr. Leon Ginzburg and Dr. Gordon D. Oppenheimer, published a landmark paper describing the features of what is known today as Crohn's disease. Crohn's and a related disease, ulcerative colitis, are the two main disease categories that belong to a larger group of illnesses called inflammatory bowel disease (IBD).

Because the symptoms of these two illnesses are so similar, it is sometimes difficult to establish the diagnosis definitively. In fact, approximately 10 percent of colitis cases are unable to be pinpointed as either ulcerative colitis or Crohn's disease and are called indeterminate colitis.

Both illnesses do have one strong feature in common. They are marked by an abnormal response by the body's immune system. The immune system is composed of various cells and proteins. Normally, these protect the body from infection. In people with Crohn's disease, however, the immune system reacts inappropriately. Researchers believe that the immune system mistakes microbes, such as bacteria that are normally found in the intestines, for foreign or invading substances, and launches an attack. In the process, the body sends white blood cells into the lining of the intestines, where they produce chronic inflammation. These cells then generate harmful products that ultimately lead to ulcerations and bowel injury. When this happens, the patient experiences the symptoms of IBD.

Although, Crohn's disease most commonly affects the end of the small intestine (the ileum) and the beginning of the large intestine (the colon), it may involve any part of the GI tract. In ulcerative colitis, on the other hand, the GI involvement is limited to the colon. In Crohn's disease, all layers of the intestine may be involved, and there can be normal healthy bowel in between patches of diseased bowel. In contrast, ulcerative colitis affects only the superficial layers (the mucosa) of the colon in a more even and continuous distribution, which starts at the level of the anus.

CCFA - The Crohn's and Colitis Foundation of America (CCFA) is a non-profit, volunteer-driven organization dedicated to finding the cure for Crohn's disease and ulcerative colitis.

Four decades ago, the Crohn's & Colitis Foundation created the field of Crohn's disease and ulcerative colitis research. Today, the Foundation funds cutting-edge studies at major medical institutions, nurtures investigators at the early stages of their careers, and finances underdeveloped areas of research. Educational workshops and symposia, together with our scientific journal, *Inflammatory Bowel Diseases*, enable medical professionals to keep pace with this rapidly growing field. No wonder the National Institutes of Health has commended the Foundation for "uniting the research community and strengthening IBD research."

CCFA Pediatric Network (PROKIIDS) - In 2007, the foremost pediatric IBD basic and clinical researchers met with the medical leadership of the Crohn's and Colitis Foundation of America (CCFA) to establish priorities in pediatric science and further pediatric IBD treatment and research. Through collaboration between the pediatric community and CCFA the Pediatric Resource Organization for Kids with Inflammatory Intestinal Diseases (PROKIIDS) was developed. The focus of PROKIIDS is to move the pediatric IBD agenda forward while building worldwide awareness around the seriousness of the issues surrounding our most vulnerable

patients. The Pediatric IBD Research Network, which falls under the PROKIDS umbrella, is a collaboration of pediatric IBD centers promoting research, education and services. Currently 29 centers around the nation are working together on research projects.

Pediatric Network - The Pediatric Network, referred to as the "Network," is a consortium of multiple centers working together on multiple research studies. All research studies to be conducted through the Network will be pre-approved by the Steering Committee, and based on study needs. Any number of the centers involved in the consortium may participate.

1. INTRODUCTION

1.1. Study Design

The currently accepted etiopathogenic hypothesis for inflammatory bowel disease proposes the role of host genetics, specifically "pre-programmed" host immune responses and environmental factors such as infectious triggers, including in particular, enteric flora, resulting in disease susceptibility, development, and eventual expression. These factors and their interactions may also be important determinants of disease phenotype and disease progression. Childhood-onset inflammatory bowel disease, Crohn's disease in particular, may be an indicator of increased genetic predisposition to develop disease, but due to other factors, may not lead to the most severe clinical course; i.e., an aggressive or complicated clinical course shown by 20-25% of subjects whom require surgery within 2 years of diagnosis. Early intervention with therapies that have the potential to alter the natural history of disease and slow down or prevent disease progression would be important. A fundamental hypothesis for this proposal is that critical clues as to environmental, genetic, and microbial factors that may mitigate the severity of disease progression may be obtained by careful comparisons of the principle attributes and characteristics across the spectrum of individual subjects. While immunomodulator and biological therapy decrease corticosteroid dependence and can improve quality of life in children with Crohn's disease, their use is not without increased risk of infection and possibly neoplasia. Thus, risk stratification of children most likely to develop complicated disease requiring more intensive therapy at the time of diagnosis using immune, genetic, and other markers and phenotypic attributes will provide both clinician and parent a better model in which to assess risk:benefit of current and emerging therapies. In this application, we propose that there are identifiable immunologic, genetic, microbial and clinical risk factors that influence the natural history of pediatric Crohn's disease. We are proposing powerful and innovative collaborative approaches that undertake a multidisciplinary research plan that will collect, correlate, and translate the new immune, host microbial ecology, genetic, and therapeutic response discoveries directly into the life of children affected with Crohn's disease. In order to accomplish our overall research objectives, we plan to study an inception cohort of 2000 well-characterized children with newly diagnosed Crohn's disease from all 29 collaborating centers participating in this project. The ultimate goals are to further develop a set of tools for understanding disease mechanism, event prognostication, and to discover and optimize individual therapeutic intervention strategies.

1.2. Study Objectives

Aim 1: To identify demographic, clinical, microbial (i.e., fecal stream characterization), genetic, and/or immunologic risk factors that influence the likelihood of the rapid development of complicated disease phenotypes manifested as, penetrating disease, stricturing disease and need for surgery in children with newly diagnosed CD. The newly formed Pediatric IBD North American Collaborative Research Group will utilize the existing participating centers in the 4 current consortia (representing 37 pediatric GI sites) and recruit additional centers (for a total of 29 sites) to enroll newly diagnosed uncomplicated (nonpenetrating-nonstricturing) pediatric CD subjects.

1a: Recruit 2000 children (age $\leq$ 16 years) with newly diagnosed Crohn's disease using standardized diagnostic criteria by collaborating with participating members of the Pediatric IBD North American Collaborative Research Group.

1b: Collect clinical and demographic information from well-characterized newly diagnosed CD subjects.

1c: Collect serum samples at diagnosis and annually for immune response testing for both current serological immune markers including ANCA, ASCA, OMPC, I2 and CBir1 and any newly identified markers.

1d: Collect and genotype samples for known candidate, novel genetic and any newly discovered variants (see methods for gene list) by high throughput SNP technology.

1e: Evaluate fresh fecal specimens by molecular methodologies (gene chip and standard fecal speciation by PCR analyses) to determine relative proportions of enteric microflora in children with newly diagnosed Crohn's disease compared to siblings and parent as representative of the index case environment.

1f: Collect mucosal biopsies in a subset inception cohort and stored for future gene expression analysis and microbial community analyses as well as standard RT-PCR for specific bacterial species.

1g: Establish a Centralized Data Coordinating Center for data collection, data quality and detailed data analyses and a Biospecimen Procurement Center and Repository to facilitate subsequent specimen analysis upon acquisition of new knowledge regarding "risk" variables.

Aim 2: Develop and validate risk stratification by stratifying subjects into different levels of risk at diagnosis based on clinical, demographic, host microbial ecology, immune and genetic determinants identified in Aim 1. The risk stratification will be completed by state-of-the-art analysis using mathematical modeling among the different risk groups of pediatric CD subjects followed over a minimum of 24 month period. Time to complication as defined by time to stricture or time to internal penetration will be included in the analysis.

2. STUDY PERSONNNEL RESPONSIBILITIES

2.1. Study Chair and Program/Site Principal Investigators

Subra Kugathasan, M.D., with Emory University is the Program PI and Study Chair overseeing all of the sites and conducting the study using good clinical practices.

This project also features two sub-projects on which Marla Dubinsky, MD, will serve as the PI for the immunogenetics component, and Lee Denson, MD will serve as the PI for the microbiological characterization component.

Site Principal Investigator

The Site Principal Investigator is responsible for the overall implementation of the study. All sites have a principal investigator that abides by good clinical practices at their site. They recruit subjects, consent, and perform the physical examinations.

2.2 Project Manager

The Project Manager located at Emory University, reports to Dr. Kugathasan and is responsible for conducting the study using good clinical practices. Responsibilities include proper implementation of the study, training of clinical personnel, oversight of study practices and procedures and coordination and dissemination of information to all participating research facilities.

Study Coordinator

The PI and/or Study Coordinator are responsible to subjects for informed consent form, performing testing, accurately recording the data, and transferring the data to the data coordination site. The study coordinator is responsible for proper documentation of adverse and serious adverse events. All study coordinators abide by good clinical practices.

2.3 Study Personnel Contact Information by Clinical Center

See 12 References for List of sites and participants

Program/Project PIs, Research Manager, Sponsor, and Data Coordinating Center Contacts
Table 1.

Steering Committee: Institute, Participant and Email/Telephone
Table 2

Table 1

Program/Project PIs, Research Manager, Sponsor, and Data Coordinating Center Contacts		
Name	Institute/Organization	Email/Telephone
Subra Kugathasan, MD Program PI and Study Chair	Emory University	skugath@emory.edu Tel: 404-727-1316 Fax: 404-727-4069
Marla Dubinsky, MD Sub-Project PI, Immunogenetics	Cedars-Sinai Medical Center	marla.dubinsky@cshs.org Tel: 310-423-7100
Lee (Ted) Denson, MD	Cincinnati Children's Hospital Medical Center	lee.denson@cchmc.org Tel: 513-696-7575
Cathy Brashear, BSN, MSN Research Project Manager	Emory University	cathy.holt.brashear@emory.edu Tel: 404-727-1190
Study Sponsor: Marjorie Merrick VP Research and Scientific Programs Saleena J. Marria MS, MBA Research Project Manager 386 Park Avenue South - 17th Fl. New York, NY 10016	Crohn's & Colitis Foundation of America	mmerrick@ccfa.org Tel: 646-943-7455 Fax: 212-779-4098 smarria@ccfa.org Tel: 646-943-7484 Fax: 212-779-4098 Website: www.ccfa.org
Data Coordinating Center (DCC): Thomas D Walters MBBS Director DCC	Hospital for Sick Children, University of Toronto CANADA	Global_DCC@prokiids.com Tel: 416-813-5143 Fax: 416-813-6531 Website: www.prokiids.com
Data Management Platform (DMP): Clint Hall Senior Project Manager 3800 Paramount Pkwy, Suite 100 Morrisville, NC 27560	Clinipace, Inc. 3800 Paramount Pkwy, Suite 100 Morrisville, NC 27560	chall@clinipace.com Tel: 919-224-8800 x 1121 Website: www.clinipace.com Fax: 919-321-2322

Table 2

Steering Committee		
Institute	**Participant**	**Email/Telephone**
Emory University	Kugathasan, Subra MD	skugath@emory.edu Tel: 404-727-1316
Cedars-Sinai Medical Center	Dubinsky, Marla MD	marla.dubinsky@cshs.org Tel: 310-423-7100
Children's Hospital of Philadelphia	Baldassano, Robert MD (Bob)	baldassano@email.chop.edu Tel: 267-426-5123
Cincinnati Children's Hospital Medical Center	Aronow, Bruce PhD	bruce.aronow@cchmc.org Tel: 513-636-0263
Cincinnati Children's Hospital Medical Center	Denson, Lee MD (Ted)	lee.denson@cchmc.org Tel: 513-636-7575
Connecticut Children's Medical Center	Hyams, Jeffery MD (Jeff)	jhyams@ccmckids.org Tel: 860-545-9532
Medical College of Wisconsin	Stephens, Michael MD (Mike)	mstephen@mcw.edu Tel: 414-266-3690
Schneider Children's Hospital	Markowitz, James MD (Jim)	jmarkowi@nshs.edu Tel: 718-470-3430
Hospital for Sick Children	Walters, Thomas MD (Tom)	thomas.walters@sickkids.ca Tel: 416-813-5143

2.4 Investigators' Meetings

Investigators' Meetings, in the form of monthly telephone conferences and Webinars, will be held to educate and train study personnel throughout the study period as needed. Annual face-to-face meetings occur at the CCFA Advances Conference. Training will include an overview of the protocols and instruction in the day-to-day activities and operations of the protocols. This includes:

- Systems requirements and navigation of the website
- Protocol Manager tool
- Review of the visit schedule and data forms
- Specimen and data collection processing and reporting
- Adverse event reporting

To obtain data of the highest quality, the study staff will be trained on completion of forms, data entry and editing procedures.

Training and certification processes are planned to ensure standardization and quality assurance. The objectives are:

- To standardize performance of key procedures from the standpoint of quality assurance so as to ensure that data is comparable, and therefore, can be used to analyze clinical findings, or endpoints of the study;
- To serve as an orientation process for personnel who will be implementing the common study protocol and performing research procedures related to it;
- To pre-test forms and procedures developed for data collection, record keeping, labeling specimens, and shipping blood samples to each of the core labs;
- To maintain a communications network between the DCC, the reference labs, and the clinical center.

Training materials will be prepared in the form of written documents or study guides. Whenever these are the most appropriate forms of media, the Data Coordinating Center (DCC) will place them on the Network web site for easy distribution. The DCC also plans to use video streaming technology on the Network web site to deliver training material. This material may be found at:

After the initial training meeting, new study personnel requiring training will be trained and certified either by in-person training at the DCC, on-site, or via a Webinar training system with the DCC or Emory Project Manager.

3. RECRUITMENT PROCEDURES AND STRATEGIES

3.1. Recruitment Strategy - General

Participants will be recruited from subjects who are evaluated, referred, and followed at the Clinical Sites. The investigator or clinical research coordinator will speak to the parent(s) or guardian(s) during clinic visits or during an inpatient admission to the hospital. The investigator

or clinical research coordinator will discuss the study design, benefits and possible risks with the family. Printed information about the study and the consent form will be given to the family.

3.2. Recruitment Strategy at Consortia/Study

Current and future clinical site subjects: Subjects will be identified by principal investigator, co-investigators, and/or research coordinator. Subjects will be identified based on a chart review of key inclusion and exclusion criteria. If subjects are found to meet inclusion/exclusion criteria their primary gastroenterologist will be consulted. If mutually agreed upon, subject will be recruited by study coordinator for study participation.

Initial contact will be made by the principal investigator or the subject's primary gastroenterologist who may or may not be a sub-investigator in the study. In some instances, initial contact will be made by the research coordinator/nurse after consulting with subject's primary gastroenterologist.

Advertising strategy for voluntary enrollments: No advertisements will be initiated.

3.3. Recruitment Goals

The goal of this study is to enroll newly-diagnosed CD subjects only. The enrollment should occur within 30 days of a diagnosis. The definition of a diagnosis is when a definitive procedure has made a solid diagnosis of CD, most often after an endoscopy or colonoscopy.

During the pilot phase among seven clinical sites, it is anticipated that about 35-50 subjects will be enrolled within the first six months. The next phases of implementation will expand the study by approximately 29 locations in several phases. The investigators are confident that the 29 sites will be able to enroll a total of 1300 newly diagnosed CD subjects who present with an uncomplicated disease phenotype: non-penetrating, nonstricturing disease. That would mean an average of about 20 new subjects per site. There will be some sites who enroll more than 20 subjects and that will balance out for the smaller sites. A cap will be set at 130 subjects per site. Every attempt should be made to recruit consecutively diagnosed subjects from each participating site to reduce the selection bias.

The individuals assessing subjects for the primary outcome (disease complications) will be blinded to information about the potential predictors such as serology and genetics. All subjects will be followed for at least 36 months. If subjects were recruited in the second year, we will request an additional year of funding to complete the follow up criteria. There are a total of 29 sites participating in this proposal. This study is strengthened by 2 additional features: 1) inclusivity: allow any interested site in North America (USA and Canada) to participate; 2) monetary reimbursement for the sites for each subject enrollment (fee for service).

3.4. Recruitment Monitoring

Research project manager at main site will monitor recruitment and enrollment for all sites through use of the Clinipace database.

3.5 Eligibility Criteria

3.5.1. Inclusion and Exclusion Criteria

3.5.1.A. Inclusion Criteria

1. Males and females ≤ 16 years of age. (Up to but not including the day of the subject's 17th Birthday).
2. A confirmed or suspected diagnosis of CD based on standardized diagnostic criteria. The enrollment visit should occur within 30 days of diagnosis.
3. Able to provide written informed consent.
4. Have consented to have specimens tested for genetics and immune responses.
5. Access to follow up data for a minimum of 36 months after diagnosis

An upper limit of 16 years of age was selected as important inclusion criteria to maximize the number of potential subjects that would be diagnosed and followed by a pediatric gastroenterologist for at least 3 years.

3.5.1.B. Exclusion Criteria

1. Infectious colitis

4. SCREENING PROCEDURES

Case Ascertainment

All subjects with a confirmed or suspected diagnosis of CD are eligible for enrollment. All investigators will have a checklist form for each potential subject to confirm eligibility

A diagnosis of CD for this study will require at least 2 of the following:
1. History of abdominal pain, weight loss, short stature, malaise, rectal bleeding or diarrhea
2. Characteristic endoscopic findings of discontinuous ulcerations, cobblestoning, fistula or severe perianal disease
3. Radiologic features of stricture, fistula, or evidence of cobblestoning or ulceration of the mucosa
4. Macroscopic appearance at laparotomy of typical bowel wall induration, mesenteric lymphadenopathy or serosal involvement showing creeping fat or other inflammatory changes
5. Histopathology showing transmural inflammatory cell infiltrate or epithelial granulomas and absence of identifiable infectious agent

5. INFORMED CONSENT

For those subjects meeting inclusion criteria, the study purpose, procedures, costs, risks, benefits and alternatives to participation will be thoroughly explained and presented to the subject and their family by the designated study coordinator and/or investigator and subjects will be screened for willingness to participate. Once subjects and families have had enough time to consider participation and have expressed a willingness to participate, informed consent will be obtained

from the parents or legal guardian and child assent when appropriate based on age and institutional IRB requirements. The signed consent allows for the collection of clinical information (subject demographics, disease phenotype), history as well as blood for genetic and immune studies from index CD cases and immediate family members. Demographic and clinical information as well as the blood collection, processing and analysis will be detailed below.

6. STUDY VISITS AND PROCEDURES

6.1. Study activities to occur at the time of subject's regularly scheduled visits for IBD care with their treatment doctor.

VISIT	1	2	3	4
Activity	Screening	12 Months	24 Months	36 Months
Informed consent process	X			
Venipuncture (12 ml screening, 12 ml annually)	X[A]	X[B]	X[B]	X[B]
Stool Collection	X[C]			
Mucosal Biopsy Collection (sub-study)[E]	X[D]			

A. 12 ml of blood (7 ml for DNA/RNA and 5 ml for serum) will be drawn at the screening visit for genetic and immune testing
B. 12 ml of blood will be drawn annually for immune testing (7 ml for DNA/RNA and 5 ml for serum)
C. 1 stool sample will be collected at screening or at follow-up if subject unable to provide at screening
D. 6 biopsy samples will be taken during regularly scheduled procedure, at time of diagnosis / screening
E. Additional biopsies will be obtained if repeat endoscopy is clinically indicated.

<u>BASELINE PROCEDURES</u>

1. Local IRB approval.

1. Subject Recruitment and Informed Consent Form

2. Detailed description in Laboratory Manual.

- <u>Blood Samples</u>. Collect 12ml of blood coinciding with routine lab work.

- <u>Stool Sample</u>. Provide stool specimen collection container to subject to collect stool specimen (1 vial, 2 ml) and store at -20˚C or below.

- <u>Mucosal Tissue Samples</u> From a subset of subjects during scheduled endoscopy, mucosal tissue biopsies (size of rice grain each) will be collected from each subject. A total of 6 biopsies will be taken: 3 each from the ileum and 3 each from the rectum.

- Register patient information by 10:00 a.m. for identification of shipped samples

3. Site to complete baseline form entitled "CD Risk Prediction: Registration and Eligibility" data case report forms (CRFs) and enter into web-based database. See Appendix B.

FOLLOW-UP PROCEDURES

4. Follow-up visits will occur every 6 months at 6, 12, 18, 24, 30 and final visit at 36 months. Study follow-up visits should occur as subject's regularly scheduled standard or care clinic visits for IBD care with their treatment doctor. If subject does not attend a clinic visit, a follow-up phone call is necessary to capture data. Sites to complete the 12 page CRF entitled "CD Risk Prediction: Data Collection at Follow-up (1) and (2)" and enter into web-based database which includes routine lab tests and treatment data. NOTE: No blood samples are required for month 6, 18 or 30, only at yearly visits.

5. At yearly 12, 24 and 36 month visit, collect 12ml of blood samples (7 ml for DNA/RNA and 5 ml for serum) of blood coinciding with routine lab work. See Lab Manual.

6.2. Case Report Forms (CRF's)

6.2.1. Completing Case Report Forms (CRFs)
The CRF forms are provided in the appendix.

The following list provides an overview of study visits and case report forms (CRFs) to be completed at each of the visits for participants.

Baseline CRF – contains the following sections:
-Registration and Eligibility
-Consent and Enrollment
-Confirmation of Diagnosis
-Demographics and History Summary
-Clinical Data at Diagnosis
-PCDAI at Diagnosis
-Location and Behaviour Data at Diagnosis
-Endoscopic Activity Score at Diagnosis
-Treatment Data at Diagnosis
-Investigation Data at Diagnosis
-Study Specific Sample Collection at Diagnosis

Follow-up CRF – contains the following sections:
-Data Collection at Follow-up
-Disease Re-assessment Data During Follow-up
-PCDAI Data at Follow-up
-Treatment & Investigation Data at Follow-up

6. SPECIMEN COLLECTION, HANDLING, AND SHIPPING

The Laboratory Manual is a guide for the collection, packaging and shipping of samples to Emory Biorepository. This manual will aid the coordinator in proper handling of samples and

provides detailed information regarding appropriate registration and notification processes for all samples.

All collection supplies, packaged sample tubes, instructions and shipping supplies are provided in advance of subject visit to each site from Emory Biorepository.

7.1 NOTIFYING THE BIOREPOSITORY OF ALL SAMPLE SHIPMENTS

Every site must notify the Emory Biorepository about the shipment of study samples.
In the first instance, this should be done online. Go to
https://prokiids.com/RISK_Shipment_Notifier.html and fill out the form on that page for each set of patient samples sent. Sample information for up to two patients may be sent with each form submission. Submission of this form will automatically notify all relevant parties about the imminent arrival of a sample. The site will receive an email acknowledging eventual receipt of the shipped sample.

In the event that the website is not available, please email the following groups:

1) Biorepository Lab Staff: Risk_lab@prokiids.com
2) Study Project Manager: Risk_pmanager@prokiids.com

Include in the **email:**

Date Sample Shipped (if other than date of email)
Site Number
FedEx tracking #
Patient Number and Samples Sent (DNA, SRM, STL, BPY, SR2, DN2, ETC)
SR2/DN2 – 12 Month, 2nd Sample
SR3/DN3 – 24 Month, 3rd Sample
SR4/DN4 – 36 Month, 4th Sample
Biopsy Location and Number of Biopsies, if sent
Comments (Please include a comment about any irregularities in shipments –
For example, "Had to write on tube and use Avery label because I didn't have the RS label."…)

SAMPLE SHIPMENT

Federal Express delivery to:
Kugathasan Lab
Emory University
Emory Children's Center
Laboratory, Room 260
2015 Uppergate Drive
Atlanta, GA 30322
404-727-9990

Pre-printed Federal Express air bills are provided.

7.2. Additional Lab Supplies
Contact Research Project Manager for additional lab supplies:
Contact Jon Waters phone 404-727-1456 jon.waters@emory.edu

8. DATA MANAGEMENT

The Data Coordinating Center (DCC) is managed by Dr Tom Walters and utilizes a Data Management Platform (DMP) hosted by Clinipace, Inc.

Role of the Data Coordinating Center

The Data Coordinating Center (DCC) was established as part of the Pediatric Research Network to support the data management and analysis of research data for the network, and to identify opportunities to implement data standards and share resources across the network. The DCC participates in the design of clinical protocols, management of the protocol and amendment approval process, in addition to providing the data management and analysis necessary to support them. It facilitates data entry by building and maintaining data entry forms. The DCC, in conjunction with Clinipace Inc, has developed and maintains the "Pro-Kiids Data Management Platform (DMP)", a clinical data management system used for the collection, storage and analysis of data for all clinical sites that participate in network studies. The DCC is responsible for generation of reports and analyzing data for this study.

The DCC also facilitates the use of appropriate technologies for communication and training, including videoconferencing and web-based video streaming, and maintains both the public and members' Web pages for the Pediatric Network (www.prokiids.com). Contact the DCC at global_DCC@prokiids.com for general questions or support issues. The DMP provider is Clinipace, Inc. (ClinipaceDMP@prokiids.com).

8.1. Introduction

The Data Platform

Clinipace, Inc. is the Data Platform Provider for this study. The data platform is a web based platform that allows users access through a single website. The platform is used for all data entry required for the projects in the Network. Clinipace is responsible for maintaining the database, for ensuring its compliance to all federal and industry standards, and ensuring its authenticity. The Data Platform will be monitored by the Data Subcommittee.

All study data is collected via systems created in collaboration with Clinipace and comply with all applicable guidelines regarding subject confidentiality and data integrity.
Registration of participants on this protocol will employ an interactive data system in which the clinical site will attest to the participant's eligibility as per protocol criteria and that an appropriate informed consent has been obtained. IRB approval for the protocol must be on file at the DCC before accrual can occur from the clinical site.

The DCC will use a system of coded identifiers to protect participant confidentiality and safety. Each participant enrolled will be assigned a local identifier by the enrollment site. This number can be a combination of the site identifier (location code) and a serial accession number. Only the registering site will have access to the linkage between this number and the personal identifiers of the participant. When the participant is registered in the study, using the DCC provided web-based registration system, the system will assign a Participant ID number. Thus each participant will have two codes; the local one that can be used by the registering site to

obtain personal identifiers, and a second code assigned by the DMP. For all data transfers to the DCC both numbers will be required to uniquely identify the participant. In this fashion, it is possible to protect against data keying errors, digit transposition or other mistakes when identifying a participant for data entry since the DCC would require that the numbers match to properly identify the participant. In this fashion, no personal identifiers would be accessible to the DCC.

8.2. Protocol Management Tools

8.2.1. Introduction

The DCC's secure web-based DMP includes the capability to capture and integrate many different forms of data. Appropriate error checking occurs as data is entered employing range and relational checks for data consistency.
User name and password: A username and password will be issued to all personnel by the DMP provider after confirmation by the DCC that the user has completed the appropriate training protocol. The user will be required to change the standard password the first time he or she logs in to the system. If you do not have or cannot remember your username or password, you can get this information by contacting your DCC study liaison (Risk_PMangaer@prokiids.com) or sending an email directly to the DMP liason staff ClinipaceDMP@prokiids.com. Please do not share your username and password. Any data entered or changed in the system will be audited by username.

8.2.2. Systems Requirements

In order to use the on-line DMP system you need to have:

Hardware and software

- Access to a PC running Windows 98, 2000, XP, or ME
- Internet Explorer 6.0 or higher.
- Internet connectivity. High-speed broadband or better connection is recommended.
- Adobe Reader is required to download some of the documents for this study. To download the Adobe Reader go to www.adobe.com and click on the *Get Adobe Reader* button.
- Software to zip/unzip files.

8.2.3. General considerations when using a web-based system

- You can access this system from any machine that has the hardware and software described above, no special installation is required.
- No intensive training needed to use this application. If you are familiar with the use of a browser you already have the basic knowledge.
- Updates to the system will be done on the server without users disruption
- The system is dependent on the Internet / Intranet for application availability. If you lose or don't have internet connectivity you won't be able to use the system.
- Web interfaces are not as mature as they are for more traditional client/server model. This means that some nice features you are used to might not be available to you.

- Most of the time you are disconnected from the server while using a web application. This means that if you close your form without clicking the *Submit* button you will lose all the information you just entered since the system won't ask (as your word processor does) if you want to save your data before closing. Also, if you don't click the *Submit* button for a period of time your session expires and you will be asked to login again. In this case, when you login again you will be able to save your work.
- It is strongly recommended that you use the navigation menus and button provided by the system instead of the Back and Forward buttons in your browser.

8.2.4. Getting Started DMP Online

The Crohn's and Colitis Foundation of America's PROKIIDS DMP is the web-based data entry site. The data entry site is hosted by Clinipace, a research software company based in Research Triangle Park, NC. Clinipace is the company; Tempo is the software. Tempo is a web based, real time workflow engine. Workflow is simply a means by which to facilitate or channel the flow of information within the system; a pathway.

8.2.5 Registering Participants and Obtaining Participant ID

Training will be conducted by telephone and webcast by the study project manager. The trainee and trainer will view a demo at the web-link. Information will be emailed to the coordinators to be trained when scheduling the appointment. The web-link is:
https://www.pediatrics.emoty.edu/20100115_CCFA01_Enrollment%20Demo.htm
After the completion of training a user name and password will be provided under two separate emails by Clinipace.

8.2.6 On-line Case Report Forms (CRF)

Data will be entered from the paper case report forms into Tempo data base hosted by Clinipace. The site can be accessed via the Pro-Kiids website (www.prokiids.com) using the "RISK Data Input" navigation button at https://prokiids.com/RISK_Public.html. Alternatively the site can be accessed directly at https://ccfaprokiids.clinipace.com/. The coordinator will obtain access to Clinipace with a user identification and password previously supplied by Clinipace. Each section of the online data base is a workflow. Workflow is simply a means to channel the flow of information into the system. The coordinators are responsible for entering the data in a timely manner. They are required to maintain current and quality data, responding to any queries of data discrepancy.

8.2.7 Data Standards

The Pro-Kiids DCC endorses the use of structured (i.e., coded) data over free-text wherever possible. Free text (i.e., uncoded) data has limited value for analysis. Where ever possible in the design of the CRFs, investigators have created structured data and avoided free text.

The DCC supports the use of standardized terminologies or classifications for data coding, and embeds tools in the online CRFs to facilitate accurate coding on demand by research staff. Where free text is collected on the CRFs, the DCC works to code the data in the current standard.

9. QUALITY ASSURANCE

9.1 Standardization

Research staff from all sites will read the Study Visit Procedures section of this Manual of Operations and will be trained to conduct visits and collect data in the same way. In addition, case report forms have been designed to minimize subjectivity and maximize standardization by requiring specific information. The study investigators are trained to conduct evaluations using published methods for performing and scoring. The same battery of tests will be used at all sites that are part of the study.

9.2 Consistency

The DCC will prepare monthly reports on the progress of the study. These reports will identify areas where data is lacking, internally inconsistent or erroneous, or falling behind the projected timeline. The investigators will act promptly to remedy any systematic barriers to the accurate and punctual transfer of data to the DCC.

9.3. Confidentiality, Security and Integrity of Data

The safety, integrity, and confidentiality of study data is protected by multiple layers of security.

1. The first layer is **physical security** (lock and key), which limits access to paper files and to computers where study information is kept to authorized staff. Each site will keep paper study records in a locked drawer or file cabinet.
2. The second layer is **logical security** (network firewalls) and is designed to allow access to the hospital/university network and to specific computers to authorized users and deny access to all others. All electronic study records will be stored on a password protected computer.

3. The third layer is **controlled access** to the Pediatric Network member website, which is managed by the DCC. Only members of the network will have access to this site, which is for member communication, protocol development, data management, sample collection management, participant management, reporting, and analysis. Access is limited to members of the network who have an assigned database account and can enter the correct user name and password for that account. All Internet communicated data developed as part of the DCC distributed data management system is transmitted over a virtual private network that is encrypted for security. The DCC makes use of secure sockets and maintains appropriate certifications for security and data confidentiality. The 128-bit level of encryption used meets current HHS standards and HIPAA regulations for clinical data.

4. The fourth layer consists of **controlling staff capabilities** within the member website. Each user must be included on the list of key staff for that study and must be assigned to a study role in order to have access to study data. If a user does not have the necessary permissions s/he will not be granted access to that study's data even if s/he has a valid password to the website but is associated with another study. Study participant confidentiality will be maintained through the use of numerically coded samples. Access to confidential

information such as names and addresses will be restricted to the research team member charged with the responsibility of following a particular subject. Several layers of password protection will strictly control all information so that only the appropriate personnel can access it at the appropriate time point in the conduct of the study. Site PIs and Coordinators will be limited to access to data entered by their site. Read access should suffice for everyone in the consortia (across each other's institutions) unless there is a documented special need for write access to more than one institution.

Further safeguards are in place to ensure the integrity of data records. In order to ensure that the correct research participant is being accessed in the research information system, authorized staff must enter 3 pieces of information: the local ID, participant ID, and site code. To protect subject confidentiality, study research data is de-identified and separated from all participants identifying information. The confidential data linking the participant to their ID is stored by the site coordinator or PI in a paper log kept under lock and key or electronically on a computer that is password-protected. Each research participant is assigned a Participant ID that can be used to link together a participant's de-identified research records but not to link directly to the confidential identifying data.

Numerous precautions have been instituted to protect the confidentiality of the data we obtain. Similar HIPAA-compliant safeguards will be implemented throughout the study.

The DCC will work closely with the study investigators to ensure that the online transmission of forms and laboratory data protects participants' confidentiality, meets IRB requirements and satisfies HIPAA regulations regarding the proper de-identification of participants.

9.4. Monitoring of Study Protocol

Checks are in place within the case report forms to help reduce the number of protocol deviations. For example:

- Coordinators review the eligibility checklist, confirming that inclusion and exclusion criteria are met, using the Eligibility Form prior to enrolling a participant in the study and continuing on to data collection.
- The on-line data capture system tracks protocol visits to ensure that visits are conducted in a timely manner.
- Case report forms are programmed to only accept study visit forms as complete if all data required by the protocol has been entered.

In addition to system checks, the Site PI regularly monitors for protocol compliance.

The DCC tracks and reports on the progress of study recruitment at each site. The DCC monitors the clinic's adherence to protocol procedure and deviations from the protocol, including enrollment of ineligible subjects. Enrollment, protocol compliance and violations are reported to the sites at least monthly.

9.5. Monitoring of Data Quality

As much as possible, data quality will be the responsibility of the study staff personnel entering the data. Data quality begins with the design of the case report forms and procedures and incorporates reasonable checks to minimize transcription and omission errors. Of the more important quality assurance measures are the internal validity checks for reasonableness and consistency. In addition to those described above, these checks may be built into the initial tables and cross tabulations that should reveal any remaining data quality issues. Only online forms will be sent to the DCC. The DCC will also provide QA reports to assess data quality after data entry.

Laboratory Data Flow. The DCC will provide a distributed data system and direct data transfer using electronic means from clinical sites, reference laboratories and radiology departments.

9.6 Monitoring of Source Documentation & Case Report Form

A number of procedures are established to ensure that the study data is of the highest quality possible. These include real-time data entry queries and data monitoring by the DCC. The DCC will also implement checks to identify forms that are due but have not been received. The DCC will be capable of automatically generating compliance report. These reports are posted monthly in the study consortia webpage. The study staff members are responsible for reviewing the compliance reports to monitor their site's compliance.

10. ADVERSE EVENTS

10.1. Definitions and Data Descriptions

Pediatric Network: multi-center consortium dedicated to sharing data through a common data platform in order to expedite research in pediatric IBD.

A *serious adverse event* includes those events that: "result in death; are life-threatening; require inpatient hospitalization or prolongation of existing hospitalization; create persistent or significant disability/incapacity, or a congenital anomaly/birth defects."

An *unexpected adverse event* is defined as any adverse experience the specificity or severity of which is not consistent with the risks of information described in the protocol. Therefore, expected adverse events are those that are identified in the research protocol as having been previously associated with or having the potential to arise as a consequence of participation in the study.

In this protocol, there are no expected adverse events. Expected symptoms and signs that are part of the disease process will not be regarded as reportable adverse events.

10.2. Reporting Requirements and Guidelines

<u>Adverse Event Reporting</u>

All adverse events (AEs) will be reviewed monthly by site PIs. If AEs occur at a high rate, a formal investigation will occur. Site PIs will report AEs to Study Chair within 60 days of occurrence.

Site PIs will report all SAE's to the Study Chair within 48 hours of occurrence. Study Chair, along with site PI, will assess causality with the study Steering Committee. If causality is determined, enrollment will be temporarily suspended until a complete investigation is conducted.

Protocol or Informed Consent Changes as a result of AEs

Within 30 days of receipt of the notification of the event, the DCC will forward summary reports of adverse event reported through this expedited system, and any amendment for the protocol and consent document that will be required. Participating sites will be required to forward these reports to their local IRB and will have 90 days from the date of receipt of this notification to obtain approval of amendment from their local IRB. Any IRB approvals for protocol amendment/informed consent changes must be transmitted via fax or email to the DCC in order to keep the protocol at that site active.

The DCC will post monthly aggregate reports of any reported adverse events to the Members website for the Study Sponsor and all site PIs.

11. REPORTING TO REGULATORY BODIES

11.1. Data and Safety Monitoring Plan (DSMP)

This study does not have a data and safety monitoring board; however, the data and safety monitoring plan is as follows:

The risks associated with this study are associated with two procedures: venipuncture and biopsy during colonoscopy. Adverse events associated with venipuncture will be monitored for by the site study coordinator, and reported to the site PI. Colonoscopies will be performed for clinical diagnostic indications in subjects with suspected CD. Adverse events will be monitored for, and managed by, the primary gastroenterologist performing the colonoscopy. These adverse events will be reported to the site PI, who will then report these to the local IRB within the time frame stipulated by the local IRB regulations. Venipuncture and mucosal biopsy sampling will be performed by medical and nursing staff with expertise in performing these procedures in children. We have used these procedures in prior and current similar studies, and anticipate that they will be quite effective in protecting the rights and welfare of the pediatric subjects.

11.2. IRB

All study sites must have Institutional Review Board (IRB) approval, prior to their initiation as required by national statutes and good clinical practice. The IRB will be given the opportunity to

monitor the progress of the study. For clinical centers, this will be their local IRB. All IRB approval letters and approved consent forms must be kept on file at both the DCC and at the clinical center. Affiliates and satellite clinics should send copies of the same IRB approval letters and consent forms to their clinical center, which is responsible for maintaining center files and for forwarding copies to the DCC. All IRB annual reports, IRB re-approval letters, and updated consent forms (with date clearly marked) must be kept on file at the clinical centers and at the DCC.

In the event such approval is not obtained and/or not forwarded to the DCC, the study may be placed on hold at the individual study site until such IRB approval has been received.

11.3. Protocol and Amendment Approvals Process

Guideline: The Project Manager will coordinate protocol amendments formally requested by the Study Chair. The procedures for coordinating these amendments may vary by the nature of the proposed amendment (substantive vs. non-substantive change).

Responsibilities:

The Study Chair is responsible for making any and all changes to the protocol documents, communicating with the research team. The Project Manager is responsible for forwarding the proposed amendment to the DCC.

The Project Manager is responsible for reviewing the completeness of the proposed amendment and communicating the current proposed amendment status to the Study Chair. The Project Manager is responsible for assigning the new protocol version date to the proposed amendment.

Procedures:

If at any time the Study Chair is ready to incorporate changes and draft an amendment to the most recently approved NIH protocol version of the protocol, the Study Chair will take the following steps:

1. Request the Word version of most recently approved protocol version from the Project Manager.

2. Advise the Project Manager of any and all identified changes into the protocol.

3. The Project Manager will prepare:
    a. Clean protocol
    b. Tracked changes protocol
    c. Summary of changes document (with rationale for changes, justification for the timing of the amendment and a description of local site IRB submission expectations)
4. The Project Manager will review the proposed amendment. If any additional modifications need to be made to the document(s), the Project Manager will send the Study Chair a list of items that need to be modified. The DCC will not modify the body

of the protocol; it is the Project Manager's responsibility (or designated staff) to modify the body any protocol that has already received approval. If no changes are identified, skip to step 6.

5. The Study Chair will utilize the tracked changes version previously sent to the DCC (step 3, above) to make additional modifications and send the proposed amendment back to the DCC (as per step 3, above).

6. Once the DCC and Study Chair are satisfied with the content of the proposed amendment, the DCC will assign the amendment a new protocol version date.

7. The proposed amendment (with new version date) will then be sent to applicable reviews (Steering Committee) as well as DCC systems group for forms/tech module/MOO impact.

Definitions:

Substantive Change: Proposed protocol changes that affect subject safety, the risk/benefit ratio to subjects, or the underlying research questions and/or study objectives.

Non-substantive Change: Proposed changes that are administrative in nature (change of contact information, grammatical corrections, etc.) that do not affect subject safety, the risk/benefit ratio to subjects, or the underlying research questions and/or study objectives.

11.4. Process of Notifying Repositories of Site Activations

Because this protocol utilizes specimen and data repositories, these institutions require copies of each DCC-activated center's IRB materials to verify appropriate consent language before specimens will be accepted. These items will be forwarded to the Project Manager by the DCC for each newly activated center in this study.

12. REFERENCES

	Site	Site Code	Principal Investigator	Coordinator
1	Emory University	emory	Subra Kugathsan	Courtney Galloway
2	Cedars-Sinai Medical	csmc	Marla Dubinsky	Shamayne Farrior
3	Children's CHOP	chop	Bob Baldassano	Ashley Martin
4	Cincinnati Children's	cchmc	Lee Denson	Katie Lake
5	Connecticut Children's	ccmc	Jeff Hyams	Miriam Lincoln
6	Medical College Wisconsin	mcw	Mike Stephens	Nicholas Peterson
7	Schneider Children's	schneider	Jim Markowitz	Kathy Grancher
8	U of California	ucsf	Mel Heyman	Deepal Dalal
9	Nationwide Children's	nationch	Wallace Crandall	Stacy Ballam
10	Harvard Children's	harchb	Johah Essers	Sarah Franklin
11	BCM-Texas Children's	bcmtch	Richard Kellermayer	Harry Siegele
12	UNC Chapel Hill	unc	Sandra Kim	Laura Walls
13	Toronto Sickkids	skto	Anne Griffiths	Karoline Fiedler
14	Goryeb Children's	gch	Joel Rush	Annette Langseder
15	IWK Health,Center	iwk	Anthony Otley	Brad MacIntyre
16	Riley Children's	rch	Mirian Pfefferkorn	Trisha Davis
17	Children's Digestive Health	ccdhc	Stanley Cohen	Tamara Wakhisi
18	Primary Children's	utah	Stephen Guthery	Ann Rutherford
19	Rhode Island Hospital	rih	Neal LeLeiko	Barb Bancroft
20	Johns Hopkins Children's	jhcc	Maria Oliva-Hemker	Vivian Abadom
21	Children's Pittsburgh	upmc	David Keljo	Sandra McRandal
22	Monroe Carell Vanderbilt	vbilt	Dedrick Moulton	Cynthia Ramirez
23	University Chicago	uoc	Barbara Kircshner	Thomas Mangatu
24	UT Southwestern	uts	Ashish Patel	Sharon Judy
25	UCLA Medical Center	uclamc	David Ziring	Emily Levy
26	Nemours Children's	nemours	Jonathan Evans	Peg Thorne
27	Women & Children's Buffalo	buffalo	Susan Baker	Christine Roach
28	Children's Denver	chd	Edward Hoffenberg	Michelle Hite
29	Children's East Ontario	cheo	David Mack	Ruth Singleton

13. STUDY CONTACTS

Role	Contact Email
Risk Study Website	https://prokiids.com/RISK_Public.html
Risk Study PI	risk_pi@prokiids.com
Risk Study Project Manager	risk_pmanager@prokiids.com
Risk Study Admin. Coordinator and Accounts	risk_admin@prokiids.com
Risk Study Bio-repository Lab Manager	risk_lab@prokiids.com
Risk Study DCC	risk_dcc@prokiids.com

Risk Study Ancillary Studies Centre	risk_ancillarystudies@prokiids.com
Risk Study Data Monitoring and Audit	risk_datamonitor@prokiids.com
CCFA VP Research and Scientific Programs	risk_ccfavp@prokiids.com
CCFA Pro-Kiids Research Project Manager	Risk_ccfapm@prokiids.com
Clinipace DMP Contact	clinipacedmp@prokiids.com
Pro-Kiids DCC	global_dcc@prokiids.com
Pro-Kiids Website	www.prokiids.com

14. SITE EMAIL CONTACTS

	Site	Principal Investigator	Coordinator
1	Emory University	risk_01emory_pi@prokiids.com	risk_01emory_coord@prokiids.com
2	Cedars-Sinai Medical	risk_02csmc_pi@prokiids.com	risk_02csmc_coord@prokiids.com
3	Children's CHOP	risk_03chop_pi@prokiids.com	risk_03chop_coord@prokiids.com
4	Cincinnati Children's	risk_04cchmc_pi@prokiids.com	risk_04cchmc_coord@prokiids.com
5	Connecticut Children's	risk_05ccmc_pi@prokiids.com	risk_05ccmc_coord@prokiids.com
6	Medical College Wisconsin	risk_06mcw_pi@prokiids.com	risk_06mcw_coord@prokiids.com
7	Schneider Children's	risk_07schneider_pi@prokiids.com	risk_07schneider_coord@prokiids.com
8	U of California	risk_08ucsf_pi@prokiids.com	risk_08ucsf_coord@prokiids.com
9	Nationwide Children's	risk_09nationch_pi@prokiids.com	risk_09nationch_coord@prokiids.com
10	Harvard Children's	risk_10harchb_pi@prokiids.com	risk_10harchb_coord@prokiids.com
11	BCM-Texas Children's	risk_11bcmtch_pi@prokiids.com	risk_11bcmtch_coord@prokiids.com
12	UNC Chapel Hill	risk_12unc_pi@prokiids.com	risk_12unc_coord@prokiids.com
13	Toronto Sickkids	risk_13skto_pi@prokiids.com	risk_13skto_coord@prokiids.com
14	Goryeb Children's	risk_14gch_pi@prokiids.com	risk_14gch_coord@prokiids.com
15	IWK Health,Center	risk_15iwk_pi@prokiids.com	risk_15iwk_coord@prokiids.com
16	Riley Children's	risk_16rch_pi@prokiids.com	risk_16rch_coord@prokiids.com
17	Children's Digestive Health	risk_17ccdhc_pi@prokiids.com	risk_17ccdhc_coord@prokiids.com
18	Primary	risk_18utah_pi@prokiids.com	risk_18utah_coord@prokiids.com

	Children's		
19	Rhode Island Hospital	risk_19rih_pi@prokiids.com	risk_19rih_coord@prokiids.com
20	Johns Hopkins Children's	risk_20jhcc_pi@prokiids.com	risk_20jhcc_coord@prokiids.com
21	Children's Pittsburgh	risk_21upmc_pi@prokiids.com	risk_21upmc_coord@prokiids.com
22	Monroe Carell Vanderbilt	risk_22vbilt_pi@prokiids.com	risk_22vbilt_coord@prokiids.com
23	University Chicago	risk_23uoc_pi@prokiids.com	risk_23uoc_coord@prokiids.com
24	UT Southwestern	risk_24uts_pi@prokiids.com	risk_24uts_coord@prokiids.com
25	UCLA Medical Center	risk_25uclamc_pi@prokiids.com	risk_25uclamc_coord@prokiids.com
26	Nemours Children's	risk_26nemours_pi@prokiids.com	risk_26nemours_coord@prokiids.com
27	Women & Children's Buffalo	risk_27buffalo_pi@prokiids.com	risk_27buffalo_coord@prokiids.com
28	Children's Denver	risk_28chd_pi@prokiids.com	risk_28chd_coord@prokiids.com
29	Children's East Ontario	risk_29cheo_pi@prokiids.com	risk_29cheo_coord@prokiids.com

APPENDIX A: CASE REPORT FORMS Version 01 Nov 2010

APPENDIX B: LABORATORY MANUAL Version 22 April 2011

CD Risk Prediction: Registration and Eligibility

1. Patient Registration for the CD Risk Prediction Study

Patient Study Registration Number ☐☐-☐☐☐ **(Affix Barcode Sticker if Available)**

***Patient First Name: _____ *Patient Family Name: _____**

***Local Hospital Record Number: _____ Local Site Identifier: _____**

**** These three (3) fields are NOT mandatory***

Year of Birth: ____ ____ ____ ____ **Gender:** *Male* *Female*

2. Reminder of Eligibility Requirements for the CD Risk Prediction Study

2.1 Is the patient younger than 17 years of age?	❑Yes	❑No	❑Unknown
2.2 Will the patient undergo upper GI endoscopy?	❑Yes	❑No	❑Unknown
2.3 Will the Ileum be visualized either radiologically and/or endoscopically?	❑Yes	❑No	❑Unknown
2.4 Do both the patient and physician anticipate that the subject will be available for follow-up at this centre for a minimum of 36 months?	❑Yes	❑No	❑Unknown
2.5 Will it be possible to obtain appropriate consent?	❑Yes	❑No	❑Unknown
2.6 Is the patient and their family willing to provide consent/assent for the collection of biological samples including DNA?	❑Yes	❑No	❑Unknown

If the response to any of the above questions is "no" or "unknown" it is likely that the subject is NOT eligible for participation in this study, please discuss with the site-PI.

3. Reminder of Exclusion Criteria for the CD Risk Prediction Study

3.1 Is the patient thought to have Ulcerative Colitis?	❑Yes	❑No	❑Unknown
3.2 At Diagnosis, is there evidence of Fibrostenotic/Penetrating Disease?	❑Yes	❑No	❑Unknown
3.3 Has the patient undergone luminal bowel resection?	❑Yes	❑No	❑Unknown
3.4 Has the patient a documented and persistent intestinal infection?	❑Yes	❑No	❑Unknown

If the response to any of the above questions is "yes", it is likely that the subject is NOT eligible for participation in this study, please discuss with the site-PI.

CD Risk Prediction: Consent and Enrollment

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

4. Study Consent Procedures

4.1 Was consent obtained ❑Yes ❑No

4.2 Date consent was obtained ___ ___ /___ ___ ___/ ___ ___ ___ ___
dd mmm yyyy

4.3 Consent Version Date ___ ___ /___ ___ ___/ ___ ___ ___ ___
dd mmm yyyy

4.4 Signee:
❑Subject ❑Mother ❑Father ❑Both Parents ❑Legal Guardian
❑Other

4.5 Was assent obtained ❑Yes ❑No

4.6 Date assent was obtained ___ ___ /___ ___ ___/ ___ ___ ___ ___
dd mmm yyyy

4.7 Assent Version Date ___ ___ /___ ___ ___/ ___ ___ ___ ___
dd mmm yyyy

5. Enrollment

***5.1* Study Enrollment Date** ___ ___ /___ ___ ___/ ___ ___ ___ ___
dd mmm yr

5a Confirmation of Enrollment Registration on Database

***5.2* Record the System Generated CD Risk Stratification Study Unique Enrollment Number here:**
(NB: This number is displayed on Workflow Number 1 "Patient Registration")

☐☐☐☐☐☐☐

(This is NOT the Patient Registration Bar-code Number or the 'Tempo' Identifier Number, but a unique number that will be provided by the DCC following registration of the patient's enrollment on the database)

Comments from Registration Process

CD Risk Prediction: Confirmation of Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

6. Does the Patient meet the study's diagnostic definition of CD?

To meet the study's definition of 'Crohn's Diease' or 'IBD-U', the subject must eventually be found to have at least ONE FEATURE from TWO of the CATEGORIES listed below.

6.1 Indicate which of the following features were apparent at the time of the patient being enrolled in this study

Y = Yes N = No U = Unknown

6.1.1) History of the following:

	Y	N	U		Y	N	U		Y	N	U
Diarrhea	❑	❑	❑	*Abdominal Pain*	❑	❑	❑	*Weight Loss*	❑	❑	❑
Rectal Bleeding	❑	❑	❑	*Malaise*	❑	❑	❑	*Linear Growth Failure*	❑	❑	❑

6.1.2) Endoscopic Findings (includes capsule endoscopy):

❑ Not available at enrollment ❑ Not available by first follow-up

	Y	N	U		Y	N	U
Discontinuous Ulcerations	❑	❑	❑	*Cobblestoning*	❑	❑	❑

6.1.3) Radiological Findings:

❑ Not available at enrollment ❑ Not available by first follow-up

	Y	N	U
Cobblestoning or ulceration of the mucosa	❑	❑	❑

6.1.4) Laparotomy Findings (NB: intestinal resection is an exclusion criteria for this study):

❑ Not applicable

	Y	N	U		Y	N	U
Typical bowel wall induration	❑	❑	❑	*Mesenteric lymphadenopathy*	❑	❑	❑
Serosa with creeping fat or other inflammatory changes	❑	❑	❑				

6.1.5) Histopathological Findings:

❑ Not available at enrollment ❑ Not available by first follow-up

	Y	N	U
Patchy inflammatory cell infiltrates	❑	❑	❑
Epithelial granuloma in the absence of identifiable infectious agents	❑	❑	❑

***6.2* At the time of enrollment, did this subject meet the study's definition of CD/IBD-U? ❑ Yes ❑ No**

If 'No":

1) ***Participants MAY continue in this study even when the requirements of the above definition are NOT met.***
2) ***Diagnostic eligibility must be reviewed again at the first follow-up visit***

***6.3* By 1st follow-up review, did this subject meet the study's definition of CD/IBD-U? ❑ Yes ❑ No**

If 'No":

If the patient does NOT fulfill the study's diagnostic definition requirements by the first follow-up visit, then it is possible that the subject is no longer eligible for participation in this study; please discuss with a Study PI.

6.4 **Name of Study PI contacted: _____ Deemed Eligible for Study?** ❑ **Yes** ❑ **No**

Comments:

CD Risk Prediction: Demographics and History Summary (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

7. Patient's Ethnic Demographics

7.1 Patient's country of birth: _____ *7.2* Estimated date of arrival in present country : ❑N/A _____

8 Family's Ethnic Demographics (in relation to the Proband)

	Stated Racial Background (textual)	*Stated Jewish Background*					*Stated Hispanic Background*		
		N	J	NA	JA	U	H	NH	U
Maternal grandmother	_____	❑	❑	❑	❑	❑	❑	❑	❑
Maternal grandfather	_____	❑	❑	❑	❑	❑	❑	❑	❑
Paternal grandmother	_____	❑	❑	❑	❑	❑	❑	❑	❑
Paternal grandfather	_____	❑	❑	❑	❑	❑	❑	❑	❑

N= not Jewish; J= Jewish (type uncertain); NA=Jewish non-Ashkenazi; JA= Jewish Ashkenazi: U=Jewish heritage status is unknown

H= Hispanic; NH= Non-Hispanic: U=Hispanic heritage status is unknown

9. Patient's Birth History

Mode of delivery:

9.1 Was the patient delivered by caesarean section? ❑Yes ❑No ❑Unknown

Patient's milk source as an infant:

9.2 Was the patient ever Breast Fed? ❑Yes ❑No ❑Unknown

If 'yes':

9.2.1 Approximate Duration of ***Exclusive*** Breastfeeding: ❑ never ❑ <1month ❑ 1-3 months ❑3-6 months ❑ >6 months

10. Patient Environmental and Medical History

Cigarette Smoke Exposure:

10.1.1 Was the patient a current smoker around the time of Dx? ❑Yes ❑No ❑Unknown

10.1.2 Did the patient live at home with a smoker anytime during the 6 month period prior to Dx? ❑Yes ❑No ❑Unknown

10.1.3 Did the patient live at home with a smoker at anytime, more than 6 months prior to Dx? ❑Yes ❑No ❑Unknown

10.1.4 Did the patient's biological mother smoke during pregnancy? ❑Yes ❑No ❑Unknown

Appendectomy:

10.2 Has the patient undergone an appendectomy? ❑Yes ❑No ❑Unknown

If 'yes':

10.2.1 Approximate date of appendectomy ____ ____ /____ ____ ____/ ____ ____ ____ ____

dd **mmm** **yyyy**

Previous Gastrointestinal Infection:

Did the patient have a severe gastrointestinal infection (eg: C difficile, Salmonella etc):

10.3.1 Within 6 months prior to Dx? ❑Yes ❑No ❑Unknown

10.3.2 At anytime more than 6 months prior to Dx? ❑Yes ❑No ❑Unknown

Non-steroidal Anti-inflammatory Drug Exposure:

10.4 Did the patient receive NSAIDs anytime during the 6 month period prior to Dx? ❑Yes ❑No ❑Unknown

If 'yes':
10.4.1 Approximate number of doses: ❑ <3 doses ❑ 3-6 doses ❑ 7-20 doses ❑ 21-30 doses ❑ >30 doses

CD Risk Prediction: Demographics and History Summary (2)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

11. Summary of Familial History of IBD

Does any member of the subject's family have a known history of IBD:

Full Sibling

Ulcerative Colitis	❑Y	❑N	❑U	❑NA	*IBD-U*	❑Y	❑N	❑U	❑NA
Crohn Disease	❑Y	❑N	❑U	❑NA	*Confirmed IBD (unaware of type)*	❑Y	❑N	❑U	❑NA

Y= Yes, N= No, U=Unknown, NA=Not Applicable (no full Siblings)

	Unknown	*No Hx of IBD*	*Ulcerative Colitis*	*Crohn Disease*	*IBD-U*	*Confirmed IBD (unaware of type)*
Mother	❑	❑	❑	❑	❑	❑
Father	❑	❑	❑	❑	❑	❑

Comments:

12. Summary of Personal and Family History

Does the patient, or any member of their family, have a known history of any of the following:

	Patient			**Full Sibling**				**Mother**			**Father**		
Atopy or Asthma	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Multiple Sclerosis	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
IDDM	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Rheumatoid Arthritis	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Lupus	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Psoriasis	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Ankylosing Spoindylitis				❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Autoimmune Thyroid Disease	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U
Celiac Disease (Bx proven)	❑Y	❑N	❑U	❑Y	❑N	❑U	❑NA	❑Y	❑N	❑U	❑Y	❑N	❑U

Y= Yes, N= No, U=Unknown, NA=Not Applicable (no full Siblings)

13. Summary of Extra Intestinal Manifestations observed in this Subject

	Recognized				Approx Date first Recognized	Comments
	Unknown	*Never*	*PreDx*	*AroundDx*		
Small Joint Arthritis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd mmm yyyy*	_____
Large Joint Arthritis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd mmm yyyy*	_____
Ankylosing Spondylitis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd mmm yyyy*	_____
Sacro-Ileitis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd mmm yyyy*	_____
Erythema Nodosum	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd mmm yyyy*	_____
Pyoderma Gangrenosum	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd mmm yyyy*	_____

Iritis/Uveitis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd* *mmm* *yyyy*	_____
Autoimmune Hepatitis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd* *mmm* *yyyy*	_____
Primary Sclerosing Cholangitis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd* *mmm* *yyyy*	_____
Pancreatitis	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ *dd* *mmm* *yyyy*	_____

Comments:

CD Risk Prediction: Clinical Data at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

14. Clinical Information at Diagnosis

14.1 Date of Diagnosis ____ ____ / ___ ___ ___ / ___ ___ ___ ___ **14.1a Age at Diagnosis**____ ____, ____ ____

dd **mmm** **yyyy** **yrs** **mths**

14.2 Diagnostic Impression at Enrollment: ❑ CD ❑ UC ❑ IBD-U ❑ Not IBD

15. Historical Anthropometric Data

Parent's Height:

Biological Mother: _____ cm
(Data unobtainable ❑)

Biological Father: _____ cm
(Data unobtainable ❑)

Patient's Growth Prior to Dx (if available):

(Data unobtainable ❑)

Date *(dd / mmm / yyyy)*	Height (cm)	Weight (kg)
__ __ / __ __ __ / __ __ __ __		
__ __ / __ __ __ / __ __ __ __		
__ __ / __ __ __ / __ __ __ __		
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__ __ / __ __ __ / __ __ __ __		

16. Patient Anthropometry at Diagnosis

16.1 Anthropometrics:

Height (cm): _____ ❑ Clinic ❑ Self-reported Weight (kg):_____ ❑ Clinic ❑ Self-reported

Date these measurements were taken ____ ____ /____ ____ ____/ ____ ____ ____ ____

dd **mmm** **yyyy**

16.2 Tanner Stage:

❑ Physician assessed ❑ Self-reported ❑ Not assessed Breasts: 1 2 3 4 5 na Pubic Hair: 1 2 3 4 5 Genitalia: 1 2 3 4 5

16.2.1 Is the Patient Post-Menarchal? ❑Not Applicable ❑Yes ❑No
❑Unknown

Estimated Date of Menarche ____ ____ /____ ____ ____/ ____ ____ ____ ____
dd mmm yyyy

17. Physician Assessment at Diagnosis

17.1 Physician Global Assessment of Disease Activity around the time of Diagnosis:

❑ None ❑ Mild ❑ Moderate ❑ Severe

(Don't forget to complete the PCDAI or PUCAI)

CD Risk Prediction: PCDAI at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

18a. Disease Activity Data Recorded at diagnosis

18.1 How was this data collected? ❑ Clinic Visit ❑ Telephone Interview ❑ Assessment not done

18.2 Date of Assessment ___ ___ / ___ ___ ___ / ___ ___ ___ ___
dd **mmm** **yyyy** **Comments:**

18.3 Which Activity Index Tool was used? ❑ PCDAI ❑ PUCAI

18b. History (Recall over past 7 days)

Most Severe Abdominal Pain
❑ None ❑ Mild: Brief, does not interfere with activities ❑ Mod/Severe: Daily, longer lasting, affects activities, nocturnal

Stools (per day)
❑ 0-1 liquid stools, no blood ❑ Up to 2 semi-formed + small blood, or 2-5 liquid +/- blood ❑ Gross bleeding, or >/= 6 liquid, or nocturnal diarrhea

Patient Functioning, General Well-being
❑ No limitation of activities, well ❑ Occasional difficulty in maintaining age appropriate activities, below par ❑ Frequent, limitation of activity very poor

18c. Examination

Weight
❑ Weight gain or voluntary weight stable/loss ❑ Involuntary weight stable, weight loss 1-9% ❑ Weight oss >/= 10%

Height
Height approximately 12 months ago: Date Taken: __ __ / __ __ __ / __ __ __ __ Height (cm) _____
d d m m m y y y y

❑ < 1 channel decrease in Ht OR Ht Vel z-score <= -1 ❑ >= 1 and < 2 channel decrease in Ht OR Ht Vel z-score -1 to <-2
❑ > 2 channel decrease in Ht OR Ht Vel z-score >= -2

Abdomen

	Yes	*No*		*Yes*	*No*		*Yes*	*No*
Tenderness	❑	❑	Mass	❑	❑	Involuntary guarding	❑	❑

Perirectal Disease

	Yes	*No*		*Yes*	*No*		*Yes*	*No*
Asymptomatic tags	❑	❑	Fissure	❑	❑	Active Fistula or abscess	❑	❑
Inflamed tags	❑	❑	Indolent fistula	❑	❑	Drainage or Tenderness	❑	❑

Extra-Intestinal Manifestations

	Yes	*No*		*Yes*	*No*		*Yes*	*No*
Fever >/= 38.5oC for 3 days over past week	❑	❑	Uveitis	❑	❑	E Nodosum	❑	❑
Oral Ulcers	❑	❑	Definite Arthritis	❑	❑	P. gangrenosum	❑	❑

18d. Investigations Required to complete Index *(Values obtained within the last week)*

	Requested	**Collected/Performed**	**Not Available**	**(Record result under "Core Investigations")**
HCT (%):	❑	❑	❑	
ESR (mm/hr):	❑	❑	❑	
Albumin (g/dL):	❑	❑	❑	

Comments:

CD Risk Prediction: PUCAI© at Diagnosis

DISREGARD this entire page if completing PCDAI form

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

18a. Disease Activity Data Recorded at diagnosis

18.1 How was this data collected? ❑ Clinic Visit ❑ Telephone Interview ❑ Assessment not done

18.2 Date of Assessment ___ ___ / ___ ___ ___ / ___ ___ ___ ___
dd **mmm** **yyyy** **Comments:**

18.3 Which Activity Index Tool was used? ❑ PCDAI ❑ PUCAI

18e. History (Last 24 hours)

1. Abdominal Pain
❑ No Pain ❑ Pain can be ignored ❑ Pain cannot be ignored

2. Rectal Bleeding
❑ None ❑ Small amount only, in less than 50% of stools

❑ Small amount with most stools ❑ Large amount (>50% of the stool content)

3. Stool Consistency of most stools
❑ Formed ❑ Partially Formed ❑ Completely unformed

4. Number of stools per 24 hours
❑ 0 – 2 ❑ 3 - 5 ❑ 6 – 8 ❑ > 8

5. Nocturnal stools (any episode causing wakening)
❑No ❑ Yes

6. Activity Level
❑ No limitation of activity ❑ Occasional limitation of activity ❑ Severely restricted activity

Comments:

CD Risk Prediction: Location and Behaviour Data at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

19. Imaging Summary around the time of Diagnosis

	NP	P		NP	P
Upper Endoscopy	❑	❑	Capsule Endoscopy	❑	❑
Lower Endoscopy (Colon)	❑	❑	Lower Endoscopy (TI)	❑	❑
UGI Series/Followthrough	❑	❑	Ba Enema	❑	❑
Abdo Ultrasound	❑	❑	Abdo CT	❑	❑
Abdo MRI	❑	❑	WCC Labeled Scan	❑	❑

NP = not performed P= performed

20. Summary of Known Disease Location around the time of Diagnosis

Please indicate disease involvement at all listed locations (tick one option only for each site)

	N	Mac	Mic	NA	U		N	Mac	Mic	NA	U
Oral	❑	❑	❑	❑	❑	Cecum	❑	❑	❑	❑	❑
Esophagus	❑	❑	❑	❑	❑	Asc Colon	❑	❑	❑	❑	❑
Stomach	❑	❑	❑	❑	❑	Trans Colon	❑	❑	❑	❑	❑
Duodenum	❑	❑	❑	❑	❑	Desc Colon	❑	❑	❑	❑	❑
Jej/Prox Ileum	❑	❑	❑	❑	❑	Sigmoid	❑	❑	❑	❑	❑
Distal Il/TI	❑	❑	❑	❑	❑	Rectum	❑	❑	❑	❑	❑

N= Normal Mac = Macroscopic disease Mic = Microscopic Disease only NA = Not Assessed U = Unknown

Comments:

21. Luminal Disease Behaviour at Diagnosis

	Yes	No	Unknown
Stricturing/Fibrostenotic	❑	❑	❑
Internally Penetrating	❑	❑	❑

If the response to either of the above questions is "yes" or "unknown" it is likely that the subject is NOT eligible for participation in this study, please discuss with the site-PI.

22. Presence of Perianal Disease around the time of Diagnosis

	Yes	No	Unknown
Large Skin Tags	❑	❑	❑
Ulcers	❑	❑	❑

Fissure/s	❑	❑	❑
Isolated Abscess	❑	❑	❑
Multiple Abscesses	❑	❑	❑
Perianal Fistula/e	❑	❑	❑
Recto-vaginal Fistula/e	❑	❑	❑
Ano-vaginal Fistula/e	❑	❑	❑

CD Risk Prediction: Endoscopic Activity Score at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

23. Endoscopy Assessment of Disease at Diagnosis (CDEIS)

Please indicate endoscopic disease involvement at all listed locations as described below

How was this data collected?

❑ Not Obtainable (Contemporaneous) ❑ Retrospective Chart Review ❑ Proceduralist (Retrospective) ❑ Proceduralist

Date of Endoscopic Assessment ___ ___ / ___ ___ ___ / ___ ___ ___ ___

dd **mmm** **yyyy**

	Assessed		Deep Ulceration		Superficial Ulceration		Amount of Surface Involved (%)	Amount of Surface Ulcerated (%)	Photo Avail		Up-loaded
	Y	N	Y	N	Y	N			N	Y	
Rectum	❑	❑	❑	❑	❑	❑	_____	_____	❑	❑	❑
Sigmoid	❑	❑	❑	❑	❑	❑	_____	_____	❑	❑	❑
Desc. Colon	❑	❑	❑	❑	❑	❑	_____	_____	❑	❑	❑
Trans. Colon	❑	❑	❑	❑	❑	❑	_____	_____	❑	❑	❑
Rgt. Colon	❑	❑	❑	❑	❑	❑	_____	_____	❑	❑	❑
Ileum	❑	❑	❑	❑	❑	❑	_____	_____	❑	❑	❑

	Y	*N*
Was there an area of ulcerated stenosis anywhere?	❑	❑
Was there an area of non-ulcerated stenosis anywhere?	❑	❑

Y= Yes N = No

Comments:

CD Risk Prediction: Treatment Data at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

24. Treatment around the time of Diagnosis

Please indicate which of the following medications were received and record the specified information

Category	Name	Received *No*	Received *Yes*	Start Date *(dd/mmm/.yyyy)*	Initial Daily Dose *(mg)*
Supplements etc					
	Probiotic Supplement	❑	❑	_____	
	Omega-3 Supplement	❑	❑	_____	
Oral 5-ASA					
	Sulfasalazine	❑	❑	_____	_____
	Mesalazine	❑	❑	_____	_____
	Olsalazine	❑	❑	_____	_____
Antibiotics					
	Metronidazole (Flagyl)	❑	❑	_____	_____
	Ciprofloxacin	❑	❑	_____	_____
	Rifaxamin (Xifaxin)	❑	❑	_____	_____
Corticosteroids					
	MethylPrednisone	❑	❑	_____	_____
	Hydrocortisone IV	❑	❑	_____	_____
	Prednisone or Prednisolone	❑	❑	_____	_____
	Oral Budesonide	❑	❑	_____	_____
Immunomodulators					
	Azathioprine	❑	❑	_____	_____
	6-Mercaptopurine	❑	❑	_____	_____
	Tacrolimus	❑	❑	_____	_____
	Cyclosporin	❑	❑	_____	_____
				Date of First Dose *(dd/mmm/.yyyy)*	**Initial Dose** *(mg)*
	Methotrexate (SC/IM)	❑	❑	_____	_____
	Methotrexate (Oral)	❑	❑	_____	_____
Biologic Agents					
	Adalimumab	❑	❑	_____	_____
	Certolizumab	❑	❑	_____	_____
	Infliximab	❑	❑	_____	_____
	Natalizumab	❑	❑	_____	_____

Enteral Therapy					Est Cal/Day *(Cal)*	Exclusive? *Excl.*	Exclusive? *Supp*
	Nutren Junior	❑	❑	_____	_____	❑	❑
	Vital Junior	❑	❑	_____	_____	❑	❑
	Pediasure	❑	❑	_____	_____	❑	❑

Ensure	❑	❑	_____	_____	❑	❑
Modulen	❑	❑	_____	_____	❑	❑
Peptamen	❑	❑	_____	_____	❑	❑
Other:	❑	❑	_____	_____	❑	❑

Comments:

CD Risk Prediction: Core Investigation Data at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

25. Summary of Core Laboratory Investigations at Diagnosis

Date of Blood Draw ____ ____ /____ ____ ____/ ____ ____ ____ ____ **Lab Used** _____

dd **mo** **yr**

	Performed			**Result**		**Performed**			**Result**
Hemoglobin (g/dL)	❑Y	❑N	❑U	_____	*CRP* (mg/L)	❑Y	❑N	❑U	_____
HCT (%)	❑Y	❑N	❑U	_____	*Albumin* (g/dL)	❑Y	❑N	❑U	_____
Platelet Count (10^9/L)	❑Y	❑N	❑U	_____	*Urea (mmol/L)*	❑Y	❑N	❑U	_____
White Cell Count (10^9/L)	❑Y	❑N	❑U	_____	*Creatinine (micromol/L)*	❑Y	❑N	❑U	_____
Neutrophil (10^9/L)	❑Y	❑N	❑U	_____	*AST (U/L)*	❑Y	❑N	❑U	_____
Lymphocytes (10^9/L)	❑Y	❑N	❑U	_____	*ALT (U/L)*	❑Y	❑N	❑U	_____
Eosinophil (10^9/L)	❑Y	❑N	❑U	_____	*Alk Phos (U/L)*	❑Y	❑N	❑U	_____
ESR (mm/hr)	❑Y	❑N	❑U	_____	*GGT (U/L)*	❑Y	❑N	❑U	_____

Y= Yes, N= No, U=Unknown

CD Risk Prediction: Study Specific Sample Collection at Diagnosis

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

26. Study Specific Investigations/Procedures to be completed this visit

Serology:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

DNA:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

Stool:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

26a. Mucosal Biopsy Sub-Study Sample Collection

Mucosal Biopsy #1:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Anatomical Site: _____

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

Mucosal Biopsy #2:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Anatomical Site: _____

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

Mucosal Biopsy #3:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Anatomical Site: _____

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

Mucosal Biopsy #4:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Anatomical Site: _____

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

Mucosal Biopsy #5:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Anatomical Site: _____

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

Mucosal Biopsy #6:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Anatomical Site: _____

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

PCDAI USER'S GUIDE

This guide is intended to help nurse coordinators and physicians complete the PCDAI in order to assess disease activity in children with Crohn's disease participating in clinical trials.

HISTORY

All calculations are based upon a 1 week (7 day) history recall of symptoms. The history recall should be solicited from the patient and/or caregiver.

1. **Abdominal pain**

The descriptions in the PCDAI of "mild" and "moderate/severe" should be used to guide in scoring the pain. Note that duration, effect on activities, and nocturnal occurrence separate moderate/severe from mild. If pain varies in severity during the week, patient should be scored according to the most severe pain. However, mild pain should be present on at least two days to score 5 points rather than 0 points.

2. Stools

The intent is to score the stool pattern during the preceding week.

To facilitate scoring, first categorize the patient as having blood in the stool or not.

If there is **no blood** in the stool, score as follows:

Formed stools or up to 1 loose stool daily = 0

2-5 liquid or very loose stools on 1 or more days = 5

6 or more liquid or very loose stools on 1 or more days or any nocturnal diarrhea = 10

If **blood** is present in the stool on any day during the past week, score as follows:

Small amounts of blood in stool (on toilet paper or small spots in stool, etc.) = 5

Any gross bleeding (large amounts on stool or colors the water in the toilet, etc.) = 10

3. Patient functioning, general well-being

If there is variation during the week, patient should be scored according to the most significant limitation of activity, even if only one day of the week, as long as likely due to Crohn's disease and not to an intercurrent illness.

PHYSICAL EXAMINATION

4.Weight (The intent is to assess the ability to normally maintain or gain weight)

Voluntary weight stable/loss means patient maintaining or losing weight on purpose.

Involuntary weight stable means patient wants to gain weight but cannot.

To calculate percentage weight loss use formula:

$$\frac{\text{Historic weight} - \text{Current weight}}{\text{Historic weight}} \times 100 = \%\ \text{weight loss}$$

Take historic weight as maximal weight attained within preceding 4-6 months, excluding any value that reflects excess weight due to corticosteroid use.

5. Height The intent is to assess the normalcy vs impairment of the patient's recent linear growth. Note that post-pubertal patients will score 0 points. For patients still growing, there are two options for scoring. Method (a) is preferred. Method (b) to be used if data required for (a) are unavailable.

a) Height velocity (cm/year), the most sensitive parameter, should be used if reliable height measurements are available from the preceding 6 to 12 months.

Convert height increment during preceding 6 to 12 months into velocity (cm/year) as follows:

$$\frac{\text{Present height} - \text{Height 6 – 12 months previously}}{\text{Interval (months) between heights}} \times 12 = \text{Height velocity (cm/year)}$$

Using height velocity chart, which accompanies PCDAI, determine centile for height velocity.

Height velocity should ideally be plotted according to bone age rather than chronologic age. However, if maturity is appropriate for age (not delayed or advanced) it is reasonable to plot and score height velocity according to chronologic age.

In follow-up visits of short-term clinical trials less than 4 months duration, score height velocity the same as the initial score unless there has been an actual height gain.

b) If reliable height measurements from 6 to 12 months previously are lacking (often the case with newly diagnosed patients), use any earlier heights to assess previous height centile and compare with current height centile. Score according to degree of decrease in height centile.

CD Risk Prediction: Data Collection at Follow-up (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

31. Data Recorded during Follow-up

Study Visit: ❑ 6mth ❑ 12mth ❑ 18mth ❑ 24mth ❑ 30mth ❑ 36mth ❑ Other _____

Date of Review: __ __ / __ __ __ / __ __ ____

32. Does the Patient meet the study's diagnostic definition of CD?

Update only if new diagnostic assessment was performed and indicate which of the following features have changed since enrolling in this study – also mark if "this is a new result at this visit." If new assessment has not been done, check "No" below and press "Next" twice in database for Workflow 2 to save as carried-forward from enrollment or previous follow-up. Proceed to section 33.

New Diagnostic Assessment was performed? ❑ ***No*** ❑ ***Yes***

32.1.2 Endoscopic Findings (includes capsule endoscopy): ❑ Not available by first follow-up

	Y	N	U
Discontinuous Ulcerations	❑	❑	❑
Cobblestoning	❑	❑	❑

❑This is a new result at this visit

❑This is a new result at this visit

32.1.3 Radiological Findings: ❑ Not available by first follow-up

	Y	N	U
Cobblestoning or ulceration of the mucosa	❑	❑	❑

❑This is a new result at this visit

32.1.4 Laparotomy Findings (NB: intestinal resection is an exclusion criteria for this study):

❑ Not available by first follow-up ❑ Not applicable

	Y	N	U
Typical bowel wall induration	❑	❑	❑
Mesenteric lymphadenopathy	❑	❑	❑

❑This is a new result at this visit

❑This is a new result at this visit

	Y	N	U
Serosa with creeping fat or other inflammatory changes	❑	❑	❑

❑ This is a new result at this visit

32.1.5 Histopathological Findings: ❑ Not available by first follow-up

	Y	N	U
Patchy inflammatory cell infiltrates	❑	❑	❑

❑ This is a new result at this visit

Epithelial granuloma in the absence of identifiable infectious agents	❑	❑	❑

❑ This is a new result at this visit

32.2 Does the subject meet the study's definition of CD/IBD-U? ❑ **Yes** ❑ **No**

32.3 If 'No":

If the patient does NOT fulfill the study's diagnostic definition requirements by the first follow-up visit, then it is possible that the subject is no longer eligible for participation in this study; please discuss with a Study PI.

32.3.1 Name of Study PI contacted: _____

32.3.2 Deemed Eligible for Study? ❑ **Yes** ❑ **No**

32.3.3 Comments:

CD Risk Prediction: Data Collection at Follow-up (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**
(Or affix Barcode Sticker if Available)

33. Data Recorded at Clinical Review following Diagnosis

33.1 Are these data taken from a clinic visit? ❑ Yes ❑ No ❑ No data are available on this participant for this review

If no data are available:

33.2 Has this Participant been permanently lost to follow-up? ❑ No ❑ Yes ❑ Uncertain

The remainder of this form cannot be completed, and should be submitted at this point.

If data are available:

33.3 Current Diagnostic Impression: ❑ CD ❑ IBD-U ❑ UC ❑ Not IBD

33.4 Has the diagnosis changed since the last review? ❑ Yes ❑ No

33.5 Anthropometrics:

Height (cm): _____ ❑ Clinic ❑ Self-reported Weight (kg):_____ ❑ Clinic ❑ Self-reported

Tanner Stage:

❑ Physician assessed ❑ Self-reported ❑ Not assessed Breasts: 1 2 3 4 5 Pubic Hair: 1 2 3 4 5 Genitalia: 1 2 3 4 5

34. Physician Assessment at this visit

34.1 Physician Global Assessment of Current Disease Activity:

❑ None ❑ Mild ❑ Moderate ❑ Severe *(Don't forget to complete the PCDAI or PUCAI)*

34.2 Physician Global Assessment of Disease Activity Since Last Review:

❑Quiescent ❑ Mild ❑ Moderate ❑ Chronically Severe ❑ Chronically Severe with remissions

If this is the first study follow-up visit (6 months), then complete the following questions, if not, move to section 35

34.2.1 What was the Participant's maximal clinical response to induction therapy by 3 months post diagnosis?

❑ Complete Response ❑ Partial Response ❑ No Response

For Patients who achieved a complete response (if 'No' or 'Partial' Response, leave this question blank)

34.2.2 Approximate time to that complete response:

❑ <1 week ❑ 1 to 2 weeks ❑ 2 to 4 weeks ❑4 to 8 weeks ❑ 8 to 12 weeks

CD Risk Prediction: Data Collection at Follow-up (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**

(Or affix Barcode Sticker if Available)

35. Review of Environmental and Disease Characteristics since last Review

Since Last Review, has the Patient:

35.2 Regularly smoked Cigarettes? ❑*No* ❑*Yes* **Lived with a person who regularly smoked Cigarettes?** ❑*No* ❑*Yes*

35.4 Undergone Luminal Surgery? ❑*No* ❑*Yes*

If yes, then complete the following information, if not, move to question 35.5

Date of Surgery: __ __ / __ __ __ / __ __ ____
dd mmm yyyy

	Yes	***No***
Procedure		
Diversion	❑	❑
Stricturoplasty	❑	❑
Luminal Resection	❑	❑
Indication		
Obstruction	❑	❑
Internal Penetration	❑	❑
Inflammatory Disease	❑	❑

35.5 Been Hospitalized related to IBD? ❑*No* ❑*Yes*

If yes, then complete the following section, if not, move to section 36

Date Admit	***Date Discharge***	***Comments***
__ __/__ __ __/__ __ __	__ __/__ __ __/__ __ __	
__ __/__ __ __/__ __ __	__ __/__ __ __/__ __ __	
__ __/__ __ __/__ __ __	__ __/__ __ __/__ __ __	
__ __/__ __ __/__ __ __	__ __/__ __ __/__ __ __	

36. Review of Family History for IBD since last Review

Please refer back to the subject's IBD Family History data recorded at the last assessment.

36.1 Are any further members of the family now known to have IBD? ❑*No* ❑*Yes*

If yes then indicate who on the following table, otherwise go directly to section 37

	Full Sibling	**Mother**	**Father**
Ulcerative Colitis	❑Y	❑Y	❑Y
Crohn Disease	❑Y	❑Y	❑Y
IBD-U	❑Y	❑Y	❑Y
Confirmed IBD (unaware of type)	❑Y	❑Y	❑Y

CD Risk Prediction: Data Collection at Follow-up (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**

(Or affix Barcode Sticker if Available)

37. Review of EIMs and other Medical Diagnoses for the Subject since last Review

Please refer back to the subject's EIM and Medical History data recorded at the last assessment.

37.1 Does the Subject report any new EIMs since the last review?

		Previously recognized?			Newly recognized since last review? (Leave blank if recognized previously)			
		Yes	*No*	*Unknown*	*No*	*Unknown*	*Yes*	Approx Date First Recognized
37.1.1	Small Joint Arthritis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.2	Large Joint Arthritis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.3	Ankylosing Spondylitis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.4	Sacro-Ileitis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.5	Erythema Nodosum	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.6	Pyoderma Gangrenosum	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.7	Iritis/Uveitis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.8	Autoimmune Hepatitis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.9	Primary Sclerosing Cholangitis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.1.10	Pancreatitis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)

37.2 Does the Subject report any new additional medical diagnoses of interest since the last review?

		Previously recognized?			Newly recognized since last review? (Leave blank if recognized previously)			
		Yes	*No*	*Unknown*	*No*	*Unknown*	*Yes*	Approx Date First Recognized
37.2.1	Rheumatoid Arthritis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.2	Psoriasis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.3	Autoimmune Thyroid Disease	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.4	Celiac Disease (Bx proven)	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.5	Atopy/Asthma	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.6	IDDM	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.7	Multiple Sclerosis	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)
37.2.8	Lupus	❑	❑	❑	❑	❑	❑	__ __ / __ __ __ / __ __ __ __ (dd / mmm / yyyy)

CD Risk Prediction: Disease Re-assessment Data During Follow-up (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**

(Or affix Barcode Sticker if Available)

38. Review of Disease Location and Behaviour since last Review

38.1 Has Disease Location/Behaviour been Reassessed since the last review? ❑ *No* ❑ *Yes*

If 'yes' complete the following questions, if 'no' then move to question 39.

38.2 Approximate Date of Reassessment: __ __ / __ __ __ / __ __ __
dd mmm yyyy

38.3 Summary of Imaging performed at this re-assessment:

	NP	P		NP	P
Upper Endoscopy	❑	❑	Capsule Endoscopy	❑	❑
Lower Endoscopy (of Colon)	❑	❑	Lower Endoscopy (of TI)	❑	❑
UGI Series/Followthrough	❑	❑	Ba Enema	❑	❑
Abdo Ultrasound	❑	❑	Abdo CT	❑	❑
Abdo MRI	❑	❑	WCC Labeled Scan	❑	❑

NP = not performed P= performed

38.4 Summary of Maximal Disease Location subsequent to the latest Re-assessment:

Please refer back to the subject's disease location data at the last assessment.

For each of the locations listed below indicate (for the current re-assessment)

1) If the location was not specifically assessed on this occasion or

2) If the level of disease involvement has increased

Tick one option only for each site. If the site was previously known to be macroscopically involved select 'unchanged'.

	NA	N	UC	Mic	Mac		NA	N	UC	Mic	Mac
Oral	❑	❑	❑	❑	❑	Cecum	❑	❑	❑	❑	❑
Esophagus	❑	❑	❑	❑	❑	Asc Col	❑	❑	❑	❑	❑
Stomach	❑	❑	❑	❑	❑	Trans Col	❑	❑	❑	❑	❑
Duodenum	❑	❑	❑	❑	❑	Desc Col	❑	❑	❑	❑	❑
Jej/Prox Ileum	❑	❑	❑	❑	❑	Sigmoid	❑	❑	❑	❑	❑
Distal Ileum/TI	❑	❑	❑	❑	❑	Rectum	❑	❑	❑	❑	❑

NA = Not Assessed N = Normal UC= Un-Changed Mic = New Microscopic Disease only Mac = New Macroscopic Disease

38.5 Stricturing/Fibrostenotic Behaviour status

Please refer back to the subject's disease behaviour data at the last assessment.

Did the participant previously exhibit Stricturing/Fibrostenotic disease behaviour? ❑ Yes ❑ No ❑ Unknown

If 'yes' then proceed to question 38.6, if 'no' or 'unknown' then answer the following question:

38.5 Does the participant now exhibit Stricturing/Fibrostenotic disease behaviou? ❑ Yes ❑ No ❑ Unknown

If 'yes' then please complete the following section, if 'no' or 'unknown' proceed to question 38.6

Approximate Date when first recognized to be present: __ __ / __ __ __ / __ __ ____
dd mmm yyyy

	Yes	No	
Features:	❑	❑	Constant luminal narrowing on DI, endo or surgery
	❑	❑	Pre-stenotic Dilatation
	❑	❑	Obstructive signs/symptoms

38.6 Internally Penetrating Behaviour status

Please refer back to the subject's disease behaviour data at the last assessment.

Did the participant previously exhibit internally penetrating disease behaviour? ❑ Yes ❑ No ❑ Unknown

If 'yes' then proceed to section 39, if 'no' or 'unknown' then answer the following question:

Does the participant now exhibit Internally Penetrating disease behaviour? ❑ Yes ❑ No ❑ Unknown

If 'yes' then please complete the following section, if 'no' or 'unknown' proceed to section 39

Approximate Date when first recognized to be present: __ __ / __ __ __ / __ __ ____
dd mmm yyyy

	Yes	No	
Features:	❑	❑	Entero-enteric or entero-vesicular fistula/e
	❑	❑	Entero-cutaneous fistula/e
	❑	❑	Intra-abdominal abscess/es
	❑	❑	Intestinal Perforation

38.7 Comments Regarding Disease Location and Behaviour Data:

CD Risk Prediction: Disease Re-assessment Data During Follow-up (2)

Patient Registration Number ❑❑-❑❑❑ **Gender:** *Male* *Female* **Study Visit:**

(Or affix Barcode Sticker if Available)

39. Update of Perianal Disease History since last Reveiw

Was it possible to obtain accurate information regarding perianal disease at this review? ❑ *No* ❑ *Yes*

If 'yes' complete the following section, if 'no' then move to section 40.

Please refer back to the subject's Perianal Disease data recorded at the last assessment.

Approximate Date of the current Perianal Review: __ __ / __ __ __ / __ __ ____
dd mmm yyyy

	Previously Recognized?			Newly Recognized Disease Since Last Review (Leave blank if previously recognized)		
	Yes	No	Unknown	Yes	No	Unknown
Large Skin Tags	❑	❑	❑	❑	❑	❑
Ulcers	❑	❑	❑	❑	❑	❑
Fissure/s	❑	❑	❑	❑	❑	❑
Isolated Abscess	❑	❑	❑	❑	❑	❑
Multiple Abscesses	❑	❑	❑	❑	❑	❑
Perianal Fistula/e	❑	❑	❑	❑	❑	❑
Recto-vaginal Fistula/e	❑	❑	❑	❑	❑	❑
Ano-vaginal Fistula/e	❑	❑	❑	❑	❑	❑

CD Risk Prediction: PCDAI Data at Follow-up

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**
(Or affix Barcode Sticker if Available)

40.1 Data Recorded at Clinical Review

How was this data collected? ❑ Clinic Visit ❑ Telephone Interview ❑ Assessment not done

Date of Assessment ___ ___ / ___ ___ ___ / ___ ___ ___ ___ **Comments:**
dd **mmm** **yyyy**

Which Activity Index Tool was used? ❑ PCDAI ❑ PUCAI

40.2 History (Recall over past 7 days)

Most Severe Abdominal Pain
❑ None ❑ Mild: Brief, does not interfere with activities ❑ Mod/Severe: Daily, longer lasting, affects activities, nocturnal

Stools (per day)
❑ 0-1 liquid stools, no blood ❑ Upto 2 semi-formed + small blood, or 2-5 liquid +/- blood ❑ Gross bleeding, or >/= 6 liquid, or nocturnal diarrhea

Patient Functioning, General Well-being
❑ No limitation of activities, well ❑ Occasional difficulty in maintaining age appropriate activities, below par ❑ Frequent, limitation of activity very poor

40.3 Examination

Weight
❑ Weight gain or voluntary weight stable/loss ❑ Involuntary weight stable, weight loss 1-9% ❑ Weight loss >/= 10%

Height
Height approximately 12 months ago: Date Taken: __ __ / __ __ __ / __ __ __ __ Height (cm) _____
d d m m m y y y y

❑ < 1 channel decrease in Ht OR Ht Vel z-score <= -1 ❑ >= 1 and < 2 channel decrease in Ht OR Ht Vel z-score -1 to <-2
❑ > 2 channel decrease in Ht OR Ht Vel z-score >= -2

Abdomen

	Yes	*No*		*Yes*	*No*		*Yes*	*No*
Tenderness	❑	❑	Mass	❑	❑	Involuntary guarding	❑	❑

Perirectal Disease

	Yes	*No*		*Yes*	*No*		*Yes*	*No*
Asymptomatic tags	❑	❑	Fissure	❑	❑	Active Fistula or abscess	❑	❑
Inflamed tags	❑	❑	Indolent fistula	❑	❑	Drainage or Tenderness	❑	❑

Extra-Intestinal Manifestations

	Yes	*No*		*Yes*	*No*		*Yes*	*No*
Fever >/= 38.5oC for 3 days over past week	❑	❑	Uveitis	❑	❑	E Nodosum	❑	❑
Oral Ulcers	❑	❑	Definite Arthritis	❑	❑	P. gangrenosum	❑	❑

40.4 Investigations Required to complete Index *(Values obtained within the last week)*

	Requested	**Collected/Performed**	**Not Available**	**(Record result under "Core Investigations")**
HCT (%):	❑	❑	❑	
ESR (mm/hr):	❑	❑	❑	
Albumin (g/dL):	❑	❑	❑	

Comments:

CD Risk Prediction: PUCAI© at Diagnosis

DISREGARD this entire page if completing PCDAI form

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female*

(Or affix Barcode Sticker if Available)

40.1. a. Disease Activity Data Recorded at diagnosis

How was this data collected? ❑ Clinic Visit ❑ Telephone Interview ❑ Assessment not done

Date of Assessment ___ ___ / ___ ___ ___ / ___ ___ ___ ___
dd **mmm** **yyyy** **Comments:**

40.1.b. History (Last 24 hours)

Abdominal Pain
❑ No Pain ❑ Pain can be ignored ❑ Pain cannot be ignored

Rectal Bleeding
❑ None ❑ Small amount only, in less than 50% of stools

❑ Small amount with most stools ❑ Large amount (>50% of the stool content)

Stool Consistency of most stools
❑ Formed ❑ Partially Formed ❑ Completely unformed

Number of stools per 24 hours
❑ 0 – 2 ❑ 3 - 5 ❑ 6 – 8 ❑ > 8

Nocturnal stools (any episode causing wakening)
❑No ❑ Yes

Activity Level
❑ No limitation of activity ❑ Occasional limitation of activity ❑ Severely restricted activity

Comments:

CD Risk Prediction: Treatment & Investigation Data at Follow-up (1)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**

(Or affix Barcode Sticker if Available)

41 Summary of Treatment since Last Review

Treatment	**Received Since Last Review?** *No*	*Yes*	**Start Date**	**Dose (mg)**	**Still Ongoing?** *No*	**Stop Date**	*Yes*	**Current Dose** **Current Daily Dose (mg)**
Supplements etc								
Probiotic	❑	❑	_____	XXXXXX	❑	_____	❑	XXXXXXXXXXXX
Omega-3	❑	❑	_____	XXXXXX	❑	_____	❑	XXXXXXXXXXXX
Oral 5-ASA								
Sulfasalazine	❑	❑	_____	_____	❑	_____	❑	_____
Mesalazine	❑	❑	_____	_____	❑	_____	❑	_____
Olsalazine	❑	❑	_____	_____	❑	_____	❑	_____
Antibiotics								
Metronidazole (Flagyl)	❑	❑	_____	_____	❑	_____	❑	_____
Ciprofloxacin	❑	❑	_____	_____	❑	_____	❑	_____
Rifaxamin (Xifaxin)	❑	❑	_____	_____	❑	_____	❑	_____
Corticosteroids								
MethylPrednisone	❑	❑	_____	_____	❑	_____	❑	_____
Hydrocortisone IV	❑	❑	_____	_____	❑	_____	❑	_____
Prednisone or Prednisolone	❑	❑	_____	_____	❑	_____	❑	_____
Oral Budesonide	❑	❑	_____	_____	❑	_____	❑	_____
Immunomodulators								
Azathioprine	❑	❑	_____	_____	❑	_____	❑	_____
6-Mercaptopurine	❑	❑	_____	_____	❑	_____	❑	_____
Tacrolimus	❑	❑	_____	_____	❑	_____	❑	_____
Cyclosporin	❑	❑	_____	_____	❑	_____	❑	_____

	Received Since Last Review? *No*	*Yes*	**Start Date**	**Dose (mg)**	**Freq**	**Still Ongoing?** *No*	**Stop Date**	*Yes*	**Change Dose or Frequency?** *No*	*Yes*	**Date**	**Dose(mg)**	**Freq**
Methotrexate (SC/IM)	❑	❑	_____	_____	_____	❑	_____	❑	❑	❑	_____	_____	____
Methotrexate (Oral)	❑	❑	_____	_____	_____	❑	_____	❑	❑	❑	_____	_____	____
Biologic Agent													
Adalimumab	❑	❑	_____	_____	_____	❑	_____	❑	❑	❑	_____	_____	____
									❑	❑	_____	_____	____
									❑	❑	_____	_____	____
									❑	❑	_____	_____	____
Certolizumab	❑	❑	_____	_____	_____	❑	_____	❑	❑	❑	_____	_____	____
									❑	❑	_____	_____	____
									❑	❑	_____	_____	____

	Received Since Last Review? *No*	*Yes*	**Start Date**	**Dose (mg)**	**Still Ongoing?** *No*	*Yes*	**Date Received**	**Dose(mg)**
Infliximab	❑	❑	_____	_____	❑	❑	_____	_____
							_____	_____
							_____	_____
							_____	_____
Natalizumab	❑	❑	_____	_____	❑	❑	_____	_____
Comments:							_____	_____

CD Risk Prediction: Treatment & Investigation Data at Follow-up (2)

Patient Registration Number ☐☐-☐☐☐ **Gender:** *Male* *Female* **Study Visit:**

(Or affix Barcode Sticker if Available)

42. Summary of Enteral Therapy since Last Review

	Received Since Last Review?				**Still Ongoing?**			**Change Dose?**			
Treatment	*No*	*Yes*	**Start Date**	**Est Cal/day**	*No*	**Stop Date**	*Yes*	*No*	*Yes*	**Date**	**Est. Cal/day)**
Exclusive											
Nutren Junior	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Vital Junior	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Pediasure	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Ensure	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Modulen	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Peptamen	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Other:											
	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Supplemental											
Nutren Junior	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Vital Junior	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Pediasure	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Ensure	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Modulen	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Peptamen	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____
Other:											
	❑	❑	_____	_____	❑	_____	❑	❑	❑	_____	_____

43. Summary of Core Laboratory Investigations at Follow-up Visit

Date of Blood Draw ____ ____ /____ ____ ____/ ____ ____ ____ ____ **Lab Used** _____

dd **mo** **yr**

	Performed			**Result**		**Performed**			**Result**
Hemoglobin (g/dL)	❑Y	❑N	❑U	_____	*CRP* (mg/L)	❑Y	❑N	❑U	_____
HCT (%)	❑Y	❑N	❑U	_____	*Albumin* (g/dL)	❑Y	❑N	❑U	_____
Platelet Count (10^9/L)	❑Y	❑N	❑U	_____	*Urea (mmol/L)*	❑Y	❑N	❑U	_____
White Cell Count (10^9/L)	❑Y	❑N	❑U	_____	*Creatinine (micromol/L)*	❑Y	❑N	❑U	_____
Neutrophil (10^9/L)	❑Y	❑N	❑U	_____	*AST (U/L)*	❑Y	❑N	❑U	_____
Lymphocytes (10^9/L)	❑Y	❑N	❑U	_____	*ALT (U/L)*	❑Y	❑N	❑U	_____
Eosinophil (10^9/L)	❑Y	❑N	❑U	_____	*Alk Phos (U/L)*	❑Y	❑N	❑U	_____
ESR (mm/hr)	❑Y	❑N	❑U	_____	*GGT (U/L)*	❑Y	❑N	❑U	_____

Y= Yes, N= No, U=Unknown

44. Study Specific Investigations/Procedures to be completed this visit

Only collected at the following reviews: **12 month** **24 month** **36 month**

Serology:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

DNA:

❑ *Will not be collected* ❑ *Requested* ❑ *Collected/performed*

Date Collected (dd/mmm/yyyy): _____ Sample ID: _____ (Barcode Identity)

PCDAI USER'S GUIDE

This guide is intended to help nurse coordinators and physicians complete the PCDAI in order to assess disease activity in children with Crohn's disease participating in clinical trials.

HISTORY

All calculations are based upon a 1 week (7 day) history recall of symptoms. The history recall should be solicited from the patient and/or caregiver.

3. **Abdominal pain**

The descriptions in the PCDAI of "mild" and "moderate/severe" should be used to guide in scoring the pain. Note that duration, effect on activities, and nocturnal occurrence separate moderate/severe from mild. If pain varies in severity during the week, patient should be scored according to the most severe pain. However, mild pain should be present on at least two days to score 5 points rather than 0 points.

4. Stools

The intent is to score the stool pattern during the preceding week.

To facilitate scoring, first categorize the patient as having blood in the stool or not.

If there is **no blood** in the stool, score as follows:

Formed stools or up to 1 loose stool daily = 0

2-5 liquid or very loose stools on 1 or more days = 5

6 or more liquid or very loose stools on 1 or more days or any nocturnal diarrhea = 10

If **blood** is present in the stool on any day during the past week, score as follows:

Small amounts of blood in stool (on toilet paper or small spots in stool, etc.) = 5

Any gross bleeding (large amounts on stool or colors the water in the toilet, etc.) = 10

3. Patient functioning, general well-being

If there is variation during the week, patient should be scored according to the most significant limitation of activity, even if only one day of the week, as long as likely due to Crohn's disease and not to an intercurrent illness.

PHYSICAL EXAMINATION

4.Weight (The intent is to assess the ability to normally maintain or gain weight)

Voluntary weight stable/loss means patient maintaining or losing weight on purpose.

Involuntary weight stable means patient wants to gain weight but cannot.

To calculate percentage weight loss use formula:

$$\frac{\text{Historic weight} - \text{Current weight}}{\text{Historic weight}} \times 100 = \%\ \text{weight loss}$$

Take historic weight as maximal weight attained within preceding 4-6 months, excluding any value that reflects excess weight due to corticosteroid use.

5. Height The intent is to assess the normalcy vs impairment of the patient's recent linear growth. Note that post-pubertal patients will score 0 points. For patients still growing, there are two options for scoring. Method (a) is preferred. Method (b) to be used if data required for (a) are unavailable.

a) Height velocity (cm/year), the most sensitive parameter, should be used if reliable height measurements are available from the preceding 6 to 12 months.

Convert height increment during preceding 6 to 12 months into velocity (cm/year) as follows:

$$\frac{\text{Present height} - \text{Height 6} - \text{12 months previously}}{\text{Interval (months) between heights}} \times 12 = \text{Height velocity (cm/year)}$$

Using height velocity chart, which accompanies PCDAI, determine centile for height velocity.

Height velocity should ideally be plotted according to bone age rather than chronologic age. However, if maturity is appropriate for age (not delayed or advanced) it is reasonable to plot and score height velocity according to chronologic age.

In follow-up visits of short-term clinical trials less than 4 months duration, score height velocity the same as the initial score unless there has been an actual height gain.

b) If reliable height measurements from 6 to 12 months previously are lacking (often the case with newly diagnosed patients), use any earlier heights to assess previous height centile and compare with current height centile. Score according to degree of decrease in height centile.

LAB MANUAL

Separate document